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(71) Applicant: ELITRA PHARMACEUTICALS, INC. [US/US]; Suite A, 3510 Dunhill Street, San Diego, CA 92121 (US).			
(72) Inventors: ZYSKIND, Judith; 8514 La Jolla Scenic Drive, La Jolla, CA 92047 (US). OHLSEN, Kari, L.; 3560 Vista De La Orilla, San Diego, CA 92117 (US). TRAWICK, John; 7210 Baldrich Street, La Mesa, CA 91942 (US). FORSYTH, R., Allyn; 1135 Beryl Street, San Diego, CA 92109 (US). FROELICH, Jamie, M.; 5057 35th Street, San Diego, CA 92116 (US). CARR, Grant, J.; 2210 Sunrise Glen, Escondido, CA 92029 (US). YAMAMOTO, Robert, T.; 3725 Norte Dame Avenue, San Diego, CA 92131 (US). XU, H., Howard; 11142 Ivy Hill Drive, San Diego, CA 92131 (US).			
(74) Agent: REISMAN, Joseph, M.; Knobbe, Martens, Olson & Bear, LLP, 16th Floor, 620 Newport Center Drive, Newport Beach, CA 92660 (US).			
(54) Title: GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN <i>ESCHERICHIA COLI</i>			
(57) Abstract <p>The sequences of nucleic acids encoding proteins required for <i>E. coli</i> proliferation are disclosed. The nucleic acids can be used to express proteins or portions thereof, to obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate molecules for rational drug discovery programs. The nucleic acids can also be used to screen for homologous genes that are required for proliferation in microorganisms other than <i>E. coli</i>. The nucleic acids can also be used to design expression vectors and secretion vectors. The nucleic acids of the present invention can also be used in various assay systems to screen for proliferation required genes in other organisms as well as to screen for antimicrobial agents.</p>			

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## GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN

*ESCHERICHIA COLI*BACKGROUND OF THE INVENTION

Since the discovery of penicillin, the use of antibiotics to treat the ravages of bacterial infections has saved millions of lives. With the advent of these "miracle drugs," for a time it was popularly believed that humanity might, once and for all, be saved from the scourge of bacterial infections. In fact, during the 1980s and early 1990s, many large pharmaceutical companies cut back or eliminated antibiotics research and development. They believed that infectious disease caused by bacteria finally had been conquered and that markets for new drugs were limited. Unfortunately, this belief was overly optimistic.

The tide is beginning to turn in favor of the bacteria as reports of drug resistant bacteria become more frequent. The United States Centers for Disease Control announced that one of the most powerful known antibiotics, vancomycin, was unable to treat an infection of the common *Staphylococcus aureus* (staph). This organism is commonly found in our environment and is responsible for many nosocomial infections. The import of this announcement becomes clear when one considers that vancomycin was used for years to treat infections caused by stubborn strains of bacteria, like staph. In short, the bacteria are becoming resistant to our most powerful antibiotics. If this trend continues, it is conceivable that we will return to a time when what are presently considered minor bacterial infections are fatal diseases.

There are a number of causes for the predicament in which practitioners of medical arts find themselves. Over-prescription and improper prescription habits by some physicians have caused an indiscriminate increase in the availability of antibiotics to the public. The patient is also partly responsible, for even in instances where an antibiotic is the appropriate treatment, patients will often improperly use the drug, the result being yet another population of bacteria that is resistant, in whole or in part, to traditional antibiotics.

The bacterial scourges that have haunted humanity remain, in spite of the development of modern scientific practices to deal with the diseases that they cause. Drug resistant bacteria are now advancing on the health of humanity. A new generation of antibiotics to once again deal with the pending health threat that bacteria present is required.

Discovery of New Antibiotics

As more and more bacterial strains become resistant to the panel of available antibiotics, new compounds are required. In the past, practitioners of pharmacology would have to rely upon traditional methods of drug discovery to generate novel, safe and efficacious compounds for the treatment of disease. Traditional drug discovery methods involve blindly testing potential drug candidate-molecules, often selected at random, in the hope that one might prove to be an effective treatment for some disease. The process is painstaking and laborious, with no guarantee of success. Today, the average cost to discover and develop a new drug is nearly US \$500 million, and the average time is 15 years from laboratory to patient. Improving this process, even incrementally, would represent a huge advance in the generation of novel antimicrobial agents.

Newly emerging practices in drug discovery utilize a number of biochemical techniques to provide for directed approaches to creating new drugs, rather than discovering them at random. For example, gene sequences and proteins encoded thereby that are required for the proliferation of an organism make for excellent targets since exposure of bacteria to compounds active against these targets would result in the inactivation of the organism. Once a target is identified, biochemical analysis of that target can be used to discover or to design molecules that interact with and alter the functions of the target. Using physical and computational techniques, to analyze structural and biochemical targets in order to derive compounds that interact with a target is called rational drug design and offers great future potential. Thus, emerging drug discovery practices use molecular modeling techniques, combinatorial chemistry approaches, and other means to produce and screen and/or design large numbers of candidate compounds.

Nevertheless, while this approach to drug discovery is clearly the way of the future, problems remain. For example, the initial step of identifying molecular targets for investigation can be an extremely time consuming task. It may also be difficult to design molecules that interact with the target by using computer modeling techniques. Furthermore, in cases where the function of the target is not known or is poorly understood, it may be difficult to design assays to detect molecules that interact with and alter the functions of the target. To improve the rate of novel drug discovery and development, methods of identifying important molecular targets in pathogenic microorganisms and methods for identifying molecules that interact with and alter the functions of such molecular targets are urgently required.

*Escherichia coli* represents an excellent model system to understand bacterial biochemistry and physiology. The estimated 4288 genes scattered along the  $4.6 \times 10^6$  base pairs of the *Escherichia coli* (*E. coli*) chromosome offer tremendous promise for the understanding of bacterial biochemical processes. In turn, this knowledge will assist in the development of new tools for the diagnosis and treatment of bacteria-caused human disease. The entire *E. coli* genome has been sequenced, and this body of information holds a tremendous potential for application to the discovery and development of new antibiotic compounds. Yet, in spite of this accomplishment, the general functions or roles of many of these genes are still unknown. For example, the total number of proliferation-required genes contained within the *E. coli* genome is unknown, but has been variously estimated at around 200 to 700 (Armstrong, K.A. and Fan, D.P. Essential Genes in the *metB-malB* Region of *Escherichia coli* K12, 1975, J. Bacteriol. 126: 48-55).

Novel, safe and effective antimicrobial compounds are needed in view of the rapid rise of antibiotic resistant microorganisms. However, prior to this invention, the characterization of even a single bacterial gene was a painstaking process, requiring years of effort. Accordingly, there is an urgent need for more novel methods to identify and characterize bacterial genomic sequences that encode gene products required for proliferation and for methods to identify molecules that interact with and alter the functions of such genes and gene products.

#### SUMMARY OF THE INVENTION

One embodiment of the present invention is a purified or isolated nucleic acid sequence consisting essentially of one of SEQ ID NOs: 1-81, 405-485, wherein said nucleic acid inhibits microorganism proliferation. The nucleic acid sequence may be complementary to at least a portion of a coding sequence of a gene whose expression is required for

microorganism proliferation. The nucleic acid sequence may comprise a fragment of one of SEQ ID NOs: 1-81, 405-485, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485. The nucleic acid sequence may be complementary to a coding sequence of a gene whose expression is required for microorganism proliferation.

Another embodiment of the present invention is a vector comprising a promoter operably linked to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 1-81, 405-485. The promoter may be active in an organism selected from the group consisting of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

Another embodiment of the present invention is a host cell containing the vectors described above.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 82-88, 90-242. One aspect of this embodiment is a fragment of the nucleic acid comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

Another embodiment of the present invention is a vector comprising a promoter operably linked to the nucleic acids of the preceding embodiment.

Another aspect of the present invention is a purified or isolated nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising a nucleic acid having at least 70% homology to a sequence selected from the group consisting of SEQ ID NOs 1-81, 405-485, 82-88, 90-242 or the sequences complementary thereto as determined using BLASTN version 2.0 with the default parameters. The nucleic acid may be from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is a host cell containing the vector of the preceding embodiment.

Another embodiment of the present invention is purified or isolated polypeptide comprising the sequence of one of SEQ ID NOs: 243-357, 359-398.

Another embodiment of the present invention is purified or isolated polypeptide comprising a fragment of one of the polypeptides of SEQ ID NOs. 243-357, 359-398, said fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the polypeptides of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is an antibody capable of specifically binding the polypeptide of the preceding embodiment.

Another embodiment of the present invention is method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 into a cell. The method may further comprise the step of isolating said protein.

Another embodiment of the present invention is a method of inhibiting proliferation comprising inhibiting the activity or reducing the amount of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

Another embodiment of the present invention is method for identifying compounds which influence the activity of a polypeptide required for proliferation comprising:

contacting a polypeptide comprising a sequence selected from the group consisting of 243-357, 359-398 with a candidate compound; and

determining whether said compound influences the activity of said polypeptide.

The activity may be an enzymatic activity. The activity may be a carbon compound catabolism activity. The activity may be a biosynthetic activity. The activity may be a transporter activity. The activity may be a transcriptional activity. The activity may be a DNA replication activity. The activity may be a cell division activity.

Another embodiment of the present invention is a compound identified using the above method.

Another embodiment of the present invention is method for assaying compounds for the ability to reduce the activity or level of a polypeptide required for proliferation, comprising:

providing a target, wherein said target comprises the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 82-88, 90-242;

contacting said target with a candidate compound; and  
measuring an activity of said target.

The target may be a messenger RNA molecule transcribed from a coding region of one of SEQ ID NOs.: 82-88, 90-242 and said activity is translation of said messenger RNA. The target may be a coding region of one of SEQ ID NOs. 82-88, 90-242 and said activity is transcription of said messenger RNA.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for identifying compounds which reduce the activity or level of a gene product required for cell proliferation comprising the steps of:

expressing an antisense nucleic acid against a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

contacting said sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

The cell may be selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells. The cell may be an *E. coli* cell. The cell may be from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The antisense nucleic acid may be transcribed from an inducible promoter. The method may, further comprise the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sublethal level. The sub-lethal concentration of said inducer may be such that growth inhibition is 8% or more. The inducer may be isopropyl-1-thio- $\beta$ -D-galactoside. The growth inhibition may be measured by monitoring optical density of a culture growth solution. The gene product may be a polypeptide. The gene product may be an RNA. The gene product may comprise a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242 or with activity against the product of said gene into a population of cells expressing a gene. The compound may be an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-81, 405-485, or a proliferation-inhibiting portion thereof. The proliferation inhibiting portion of one of SEQ ID NOs. 1-81, 405-485

may be a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485. The compound may be a triple helix oligonucleotide.

Another embodiment of the present invention is a preparation comprising an effective concentration of an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-81, 405-485, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier. The proliferation-inhibiting portion of one of SEQ ID NOs. 1-81, 405-485 may comprise at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485.

Another embodiment of the present invention is a method for inhibiting the expression of a gene in an operon required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid, said cell expressing a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242, wherein said antisense nucleic acid comprises at least a proliferation-inhibiting portion of said operon in an antisense orientation that is effective in inhibiting expression of said gene. The antisense nucleic acid may be complementary to a sequence of a gene comprising one or more of SEQ ID NOs.: 82-88, 90-242. The antisense nucleic acid may be a sequence of one of SEQ ID NOs.: 1-81, 405-485, or a portion thereof. The cell may be contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a sequence encoding said antisense nucleic acid into the chromosome of said cell into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a retran which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a ribozyme into said cell population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide. The cell may be contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell. The cell may be contacted with said antisense nucleic acid by electroporation. The antisense nucleic acid may be a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242. The antisense nucleic acid may be an oligonucleotide.

Another embodiment of the present invention is a method for identifying bacterial strains comprising the steps of:

providing a sample containing a bacterial species; and

identifying a bacterial species using a species specific probe having a sequence selected from the group consisting of SEQ ID NOs. 1-81, 405-485, 82-88, 90-242.

Another embodiment of the present invention is a method for identifying a gene in a microorganism required for proliferation comprising:

(a) identifying an inhibitory nucleic acid which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with said inhibitory nucleic acid;

- (c) determining whether said inhibitory nucleic acid from said first microorganism inhibits proliferation of said second microorganism; and
- (d) identifying the gene in said second microorganism which is inhibited by said inhibitory nucleic acid.

Another embodiment of the present invention is a method for assaying a compound for the ability to inhibit proliferation of a microorganism comprising:

- (a) identifying a gene or gene product required for proliferation in a first microorganism;
- (b) identifying a homolog of said gene or gene product in a second microorganism;
- (c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;
- (d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
- (e) contacting the sensitized microorganism of step (d) with a compound; and
- (f) determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

The step of identifying a gene involved in proliferation in a first microorganism may comprise:

introducing a nucleic acid comprising a random genomic fragment from said first microorganism operably linked to a promoter wherein said random genomic fragment is in the antisense orientation; and

comparing the proliferation of said first microorganism transcribing a first level of said random genomic fragment to the proliferation of said first microorganism transcribing a lower level of said random genomic fragment, wherein a difference in proliferation indicates that said random genomic fragment comprises a gene involved in proliferation.

The step of identifying a homolog of said gene in a second microorganism may comprise identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a database using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters. The step of identifying a homolog of said gene in a second microorganism may comprise identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene. The step of identifying a homolog of said gene in a second microorganism may comprise expressing a nucleic acid which inhibits the proliferation of said first microorganism in said second microorganism. The inhibitory nucleic acid may be an antisense nucleic acid. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of said homolog. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of the operon encoding said homolog. The step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence may comprise directly contacting said second microorganism with said nucleic acid. The step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence may comprise expressing an antisense nucleic acid to said homolog in said second microorganism.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method of assaying a compound for the ability to inhibit proliferation comprising:

- (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;
- (b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
- (c) contacting the proliferation-inhibited microorganism of step (b) with a compound; and
- (d) determining whether said compound inhibits proliferation of said sensitized second microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized second microorganism.

The inhibitory nucleic acid may be an antisense nucleic acid which inhibits the proliferation of said first microorganism. The inhibitory nucleic acid may comprise a portion of an antisense nucleic acid which inhibits the proliferation of said first microorganism. The inhibitory nucleic acid may comprise an antisense molecule against the entire coding region of the gene involved in proliferation of the first microorganism. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of the operon encoding the gene involved in proliferation of the first microorganism.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for assaying compounds for activity against a biological pathway required for proliferation comprising:

- sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;
- contacting the sensitized cell with a compound; and
- determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

The cell may be selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells. The cell may be an *E. coli* cell. The cell may be an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The antisense nucleic acid may be transcribed from an inducible promoter. The method may further comprise contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sublethal level. The sublethal level of said antisense nucleic acid



may inhibit proliferation by 8% or more. The agent may be isopropyl-1-thio- $\beta$ -D-galactoside (IPTG). The inhibition of proliferation may be measured by monitoring the optical density of a liquid culture. The gene product may comprise a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

Another embodiment of the present invention is a compound identified using the method above.

5. Another embodiment of the present invention is a method for assaying a compound for the ability to inhibit cellular proliferation comprising:

contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

contacting said cell with said compound; and

10 determining whether said compound reduces proliferation to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

The agent which reduces the activity or level of a gene product required for proliferation of said cell may comprise an antisense nucleic acid to a gene or operon required for proliferation. The agent which reduces the activity or level of a gene product required for proliferation of said cell may comprise an antibiotic. The cell may contain a  
15 temperature sensitive mutation which reduces the activity or level of said gene product required for proliferation of said cell. The antisense nucleic acid may be directed against the same functional domain of said gene product required for proliferation of said cell to which said antisense nucleic acid is directed. The antisense nucleic acid may be directed against a different functional domain of said gene product required for proliferation of said cell than the functional domain to which said antisense nucleic acid is directed.

20 Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for identifying the pathway in which a proliferation-required nucleic acid or its gene product lies comprising:

expressing a sublethal level of an antisense nucleic acid directed against said proliferation-required nucleic acid in a cell;

25 contacting said cell with an antibiotic, wherein the a biological pathway on which said antibiotic acts is known; and

determining whether said cell has a substantially greater sensitivity to said antibiotic than a cell which does not express said sublethal level of said antisense nucleic acid.

Another embodiment of the present invention is a method for determining the pathway on which a test  
30 compound acts comprising:

(a) expressing a sublethal level of an antisense nucleic acid directed against a proliferation-required nucleic acid in a cell, wherein the biological pathway in which said proliferation-required nucleic acid lies is known,

(b) contacting said cell with said test compound; and

35 (c) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

The method may further comprise:

(d) expressing a sublethal level of a second antisense nucleic acid directed against a second proliferation-required nucleic acid in said cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

(e) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of one of SEQ ID NOs: 358, 399-402.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising a sequence selected from the group consisting of 1-81, 405-485, 82-88, 90-242, 358, 399-402.

Another embodiment of the present invention is a compound which interacts with the gene or gene product of a nucleic acid comprising a sequence of one of SEQ ID NOs: 82-88, 90-242 to inhibit proliferation.

Another embodiment of the present invention compound which interacts with a polypeptide comprising one of SEQ ID NOs. 243-357, 359-398 to inhibit proliferation.

Another embodiment of the present invention is a compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an IPTG dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing either an antisense clone to the *E. coli* ribosomal protein rplW (AS-rplW) which is required for protein synthesis and essential cell proliferation, or an antisense clone to the *elaD* (AS-*elaD*) gene which is not known to be involved in protein synthesis and which is also essential for proliferation.

Figure 2A is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to rplW(AS-rplW) in the presence of 0, 20 or 50  $\mu$ M IPTG.

Figure 2B is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to *elaD* (AS-*elaD*) in the presence of 0, 20 or 50  $\mu$ M IPTG.

Figure 3 is a graph showing the fold increase in tetracycline sensitivity of *E. coli* transfected with antisense clones to essential ribosomal proteins L23 (AS-rplW) and L7/L12 and L10 (AS-rplLrplJ). Antisense clones to genes known not to be involved in protein synthesis (*atpB/E*(AS-*atpB/E*), *visC* (AS-*visC*, *elaD* (AS-*elaD*), *yohH* (AS-*yohH*)) are much less sensitive to tetracycline.

#### Definitions

By "biological pathway" is meant any discrete cell function or process that is carried out by a gene product or a subset of gene products. Biological pathways include enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such cell walls. Biological pathways that are usually required for proliferation of microorganisms include, but are not limited to, cell division, DNA synthesis & replication,

RNA synthesis (transcription), protein synthesis (translation), protein processing, protein transport, fatty acid biosynthesis, cell wall synthesis, cell membrane synthesis & maintenance, etc.

By "inhibit activity against a gene or gene product" is meant having the ability to interfere with the function of a gene or gene product in such a way as to decrease expression of the gene or to reduce the level or activity of a product of the gene. Agents which have activity against a gene include agents that inhibit transcription of the gene and agents that inhibit translation of the mRNA transcribed from the gene. In microorganisms, agents which have activity against a gene can act to decrease expression of the operon in which the gene resides or alter the processing of operon RNA such as to reduce the level or activity of the gene product. The gene product can be a non-translated RNA such as ribosomal RNA, a translated RNA (mRNA) or the protein product resulting from translation of the gene mRNA. Of particular utility to the present invention are anti-sense RNAs that have activities against the operons or genes to which they specifically hybridize.

By "activity against a gene product" is meant having the ability to inhibit the function or to reduce the level or activity of the gene product in a cell.

By "activity against a protein" is meant having the ability to inhibit the function or to reduce the level or activity of the protein in a cell.

By "activity against nucleic acid" is meant having the ability to inhibit the function or to reduce the level or activity of the nucleic acid in a cell.

As used herein, "sublethal" means a concentration of an agent below the concentration required to inhibit all cell growth.

#### DETAILED DESCRIPTION OF THE INVENTION

The present invention describes a group of *E. coli* genes and gene families required for growth and/or proliferation. A proliferation-required gene or gene family is one where, in the absence of a gene transcript and/or gene product, growth or viability of the microorganism is reduced or eliminated. Thus, as used herein the terminology "proliferation-required" or "required for proliferation" encompasses sequences where the absence of a gene transcript and/or gene product completely eliminates cell growth as well as sequences where the absence of a gene transcript and/or gene product merely reduces cell growth. These proliferation-required genes can be used as potential targets for the generation of new antimicrobial agents. To achieve that goal, the present invention also encompasses novel assays for analyzing proliferation-required genes and for identifying compounds which interact with the gene products of the proliferation-required genes. In addition, the present invention contemplates the expression of genes and the purification of the proteins encoded by the nucleic acid sequences identified as required proliferation genes and reported herein. The purified proteins can be used to generate reagents and screen small molecule libraries or other candidate compound libraries for compounds that can be further developed to yield novel antimicrobial compounds. The present invention also describes methods for identification of homologous genes in organisms other than *E. coli*.

The present invention utilizes a novel method to identify proliferation-required *E. coli* sequences. Generally, a library of nucleic acid sequences from a given source are subcloned or otherwise inserted into an inducible expression

vector, thus forming an expression library. Although the insert nucleic acids may be derived from the chromosome of the organism into which the expression vector is to be introduced, because the insert is not in its natural chromosomal location, the insert nucleic acid is an exogenous nucleic acid for the purposes of the discussion herein. The term expression is defined as the production of an RNA molecule from a gene, gene fragment, genomic fragment, or operon. Expression can also be used to refer to the process of peptide or polypeptide synthesis. An expression vector is defined as a vehicle by which a ribonucleic acid (RNA) sequence is transcribed from a nucleic acid sequence carried within the expression vehicle. The expression vector can also contain features that permit translation of a protein product from the transcribed RNA message expressed from the exogenous nucleic acid sequence carried by the expression vector. Accordingly, an expression vector can produce an RNA molecule as its sole product or the expression vector can produce a RNA molecule that is ultimately translated into a protein product.

Once generated, the expression library containing the exogenous nucleic acid sequences is introduced into an *E. coli* population to search for genes that are required for bacterial proliferation. Because the library molecules are foreign to the population of *E. coli*, the expression vectors and the nucleic acid segments contained therein are considered exogenous nucleic acid.

Expression of the exogenous nucleic acid fragments in the test population of *E. coli* containing the expression vector library is then activated. Activation of the expression vectors consists of subjecting the cells containing the vectors to conditions that result in the expression of the exogenous nucleic acid sequences carried by the expression vector library. The test population of *E. coli* cells is then assayed to determine the effect of expressing the exogenous nucleic acid fragments on the test population of cells. Those expression vectors that, upon activation and expression, negatively impact the growth of the *E. coli* screen population were identified, isolated, and purified for further study.

A variety of assays are contemplated to identify nucleic acid sequences that negatively impact growth upon expression. In one embodiment, growth in *E. coli* cultures expressing exogenous nucleic acid sequences and growth in cultures not expressing these sequences is compared. Growth measurements are assayed by examining the extent of growth by measuring optical densities. Alternatively, enzymatic assays can be used to measure bacterial growth rates to identify exogenous nucleic acid sequences of interest. Colony size, colony morphology, and cell morphology are additional factors used to evaluate growth of the host cells. Those cultures that failed to grow or grow with reduced efficiency under expression conditions are identified as containing an expression vector encoding a nucleic acid fragment that negatively affects a proliferation-required gene.

Once exogenous nucleic acid sequences of interest are identified, they are analyzed. The first step of the analysis is to acquire the nucleic acid sequence of the nucleic acid fragment of interest. To achieve this end, the insert in those expression vectors identified as containing a sequence of interest is sequenced, using standard techniques well known in the art. The next step of the process is to determine the source of the nucleic acid sequence.

Determination of sequence source is achieved by comparing the obtained sequence data with known sequences in various genetic databases. The sequences identified are used to probe these gene databases. The result of this

procedure is a list of exogenous nucleic acid sequences corresponding to a list that includes novel bacterial genes required for proliferation as well as genes previously identified as required for proliferation.

The number of DNA and protein sequences available in database systems has been growing exponentially for years. For example, at the end of 1998, the complete sequences of *Caenorhabditis elegans*, *Saccharomyces cerevisiae* and nineteen bacterial genomes, including *E. coli* were available. This sequence information is stored in a number of databanks, such as GenBank (the National Center for Biotechnology Information (NCBI), and is publicly available for searching.

A variety of computer programs are available to assist in the analysis of the sequences stored within these databases. FastA, (W. R. Pearson (1990) "Rapid and Sensitive Sequence Comparison with FASTP and FASTA" Methods in Enzymology 183:63- 98), Sequence Retrieval System (SRS), (Etzold & Argos, SRS an indexing and retrieval tool for flat file data libraries. Comput. Appl. Biosci. 9:49-57, 1993) are two examples of computer programs that can be used to analyze sequences of interest. In one embodiment of the present invention, the BLAST family of computer programs, which includes BLASTN version 2.0 with the default parameters, or BLASTX version 2.0 with the default parameters, is used to analyze nucleic acid sequences.

BLAST, an acronym for "Basic Local Alignment Search Tool," is a family of programs for database similarity searching. The BLAST family of programs includes: BLASTN, a nucleotide sequence database searching program, BLASTX, a protein database searching program where the input is a nucleic acid sequence; and BLASTP, a protein database searching program. BLAST programs embody a fast algorithm for sequence matching, rigorous statistical methods for judging the significance of matches, and various options for tailoring the program for special situations. Assistance in using the program can be obtained by e-mail at [blast@ncbi.nlm.nih.gov](mailto:blast@ncbi.nlm.nih.gov).

Bacterial genes are often transcribed in polycistronic groups. These groups comprise operons, which are a collection of genes and intergenic sequences. The genes of an operon are co-transcribed and are often related functionally. Given the nature of the screening protocol, it is possible that the identified exogenous nucleic acid sequence corresponds to a gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual sequence that is required for bacterial proliferation. Accordingly, determining which of the genes that are encoded within the operons are individually required for proliferation is often desirable.

In one embodiment of the present invention, an operon is dissected to determine which gene or genes are required for proliferation. For example, the RegulonDB DataBase described by Huerta et al. (*Nucl. Acids Res.* 26:55-59, 1998), which may also be found on the website [http://www.cifn.unam.mx/Computational\\_Biology/regulondb/](http://www.cifn.unam.mx/Computational_Biology/regulondb/), may be used to identify the boundaries of operons encoded within microbial genomes. A number of techniques that are well known in the art can be used to dissect the operon. In one aspect of this embodiment, gene disruption by homologous recombination is used to individually inactivate the genes of an operon that is thought to contain a gene required for proliferation.

Several gene disruption techniques have been described for the replacement of a functional gene with a mutated, non-functional (null) allele. These techniques generally involve the use of homologous recombination. The

method described by Link et al. (J. Bacteriol 1997 179:6228; incorporated herein by reference in it's entirety) serves as an excellent example of these methods as applicable to disruption of genes in *E. coli*. This technique uses crossover PCR to create a null allele with an in-frame deletion of the coding region of a target gene. The null allele is constructed in such a way that sequences adjacent to the wild type gene (ca. 500 bp) are retained. These homologous sequences surrounding the deletion null allele provide targets for homologous recombination so that the wild type gene on the *E. coli* chromosome can be replaced by the constructed null allele.

The crossover PCR amplification product is subcloned into the vector pK03, the features of which include a chloramphenicol resistance gene, the counter-selectable marker *sacB*, and a temperature sensitive autonomous replication function. Following transformation of an *E. coli* cell population with such a vector, selection for cells that have undergone homologous recombination of the vector into the chromosome is achieved by growth on chloramphenicol at the non-permissive temperature of 43°C. Under these conditions, autonomous replication of the plasmid cannot occur and cell are resistant to chloramphenicol only if the chloramphenicol resistance gene has been integrated into the chromosome. Usually a single crossover event is responsible for this integration event such that the *E. coli* chromosome now contains a tandem duplication of the target gene consisting of one wild type allele and one deletion null allele separated by vector sequence.

This new *E. coli* strain containing the tandem duplication can be maintained at permissive temperatures in the presence of drug selection (chloramphenicol). Subsequently, cells of this new strain are cultured at the permissive temperature 30°C without drug selection. Under these conditions, the chromosome of some of the cells within the population will have undergone an internal homologous recombination event resulting in removal of the plasmid sequences. Subsequent culturing of the strain in growth medium lacking chloramphenicol but containing sucrose is used to select for such recombinative resolutions. In the presence of the counter-selectable marker *sacB*, sucrose is rendered into a toxic metabolite. Thus, cells that survive this counter-selection have lost both the plasmid sequences from the chromosome and the autonomously replicating plasmid that results as a byproduct of recombinative resolution.

There are two possible outcomes of the above recombinative resolution via homologous recombination. Either the wild type copy of the targeted gene is retained on the chromosome or the mutated null allele is retained on the chromosome. In the case of an essential gene, a single copy of the null allele would be lethal and such cells should not be obtained by the above procedure when applied to essential genes. In the case of a non-essential gene, roughly equal numbers of cells containing null alleles and cells containing wild type alleles should be obtained. Thus, the method serves as a test for essentiality of the targeted gene: when applied to essential genes, only cells with a wild type allele on the chromosome will be obtained.

Other techniques have also been described for the creation of disruption mutations in *E. coli*. For example, Link et al. also describe inserting an in-frame sequence tag concomitantly with an in-frame deletion in order to simplify analysis of recombinants obtained. Further, Link et al. describe disruption of genes with a drug resistance marker such as a kanamycin resistance gene. Arigoni et al., (Arigoni, F. et al. A Genome-based Approach for the

Identification of Essential Bacterial Genes, Nature Biotechnology 16: 851-856, the disclosure of which is incorporated herein by reference in its entirety) describe the use of gene disruption combined with engineering a second copy of a test gene such that the expression of the gene is regulated by and inducible promoter such as the arabinose promoter to test the essentiality of the gene. Many of these techniques result in the insertion of large fragments of DNA into the gene of interest, such as a drug selection marker. An advantage of the technique described by Link et al. is that it does not rely on an insertion into the gene to cause a functional defect, but rather results in the precise removal of the coding region. This insures the lack of polar effects on the expression of genes downstream from the target gene.

Recombinant DNA techniques can be used to express the entire coding sequences of the gene identified as required for proliferation, or portions thereof. The over-expressed proteins can be used as reagents for further study. The identified exogenous sequences are isolated, purified, and cloned into a suitable expression vector using methods well known in the art. If desired, the nucleic acids can contain the sequences encoding a signal peptide to facilitate secretion of the expressed protein.

Expression of fragments of the bacterial genes identified as required for proliferation is also contemplated by the present invention: The fragments of the identified genes can encode a polypeptide comprising at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 75, or more than 75 consecutive amino acids of a gene complementary to one of the identified sequences of the present invention. The nucleic acids inserted into the expression vectors can also contain sequences upstream and downstream of the coding sequence.

When expressing the coding sequence of an entire gene identified as required for bacterial proliferation or a fragment thereof, the nucleic acid sequence to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector can be any of the bacterial, insect, yeast, or mammalian expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon usage and codon bias of the sequence can be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, et al., U.S. Patent No. 5,082,767, incorporated herein by this reference. Fusion protein expression systems are also contemplated by the present invention.

Following expression of the protein encoded by the identified exogenous nucleic acid sequence, the protein is purified. Protein purification techniques are well known in the art. Proteins encoded and expressed from identified exogenous nucleic acid sequences can be partially purified using precipitation techniques, such as precipitation with polyethylene glycol. Chromatographic methods usable with the present invention can include ion-exchange chromatography, gel filtration, use of hydroxyapatite columns, immobilized reactive dyes, chromatofocusing, and use of high-performance liquid chromatography. Electrophoretic methods such one-dimensional gel electrophoresis, high-resolution two-dimensional polyacrylamide electrophoresis, isoelectric focusing, and others are contemplated as purification methods.

Also, affinity chromatographic methods, comprising antibody columns, ligand presenting columns and other affinity chromatographic matrices are contemplated as purification methods in the present invention.

The purified proteins produced from the gene coding sequences identified as required for proliferation can be used in a variety of protocols to generate useful antimicrobial reagents. In one embodiment of the present invention, antibodies are generated against the proteins expressed from the identified exogenous nucleic acid sequences. Both monoclonal and polyclonal antibodies can be generated against the expressed proteins. Methods for generating monoclonal and polyclonal antibodies are well known in the art. Also, antibody fragment preparations prepared from the produced antibodies discussed above are contemplated.

Another application for the purified proteins of the present invention is to screen small molecule libraries for candidate compounds active against the various target proteins of the present invention. Advances in the field of combinatorial chemistry provide methods, well known in the art, to produce large numbers of candidate compounds that can have a binding, or otherwise inhibitory effect on a target protein. Accordingly, the screening of small molecule libraries for compounds with binding affinity or inhibitory activity for a target protein produced from an identified gene sequence is contemplated by the present invention.

The present invention further contemplates utility against a variety of other pathogenic organisms in addition to *E. coli*. For example, the invention has utility in identifying genes required for proliferation in prokaryotes and eukaryotes. For example, the invention has utility with protists, such as *Plasmodium* spp.; plants; animals, such as *Entamoeba* spp. and *Contracaecum* spp; and fungi including *Candida* spp., (e.g., *Candida albicans*), *Saccharomyces cerevisiae*, *Cryptococcus neoformans*, and *Aspergillus fumigatus*. In one embodiment of the present invention, monera, specifically bacteria are probed in search of novel gene sequences required for proliferation. This embodiment is particularly important given the rise of drug resistant bacteria.

The numbers of bacterial species that are becoming resistant to existing antibiotics are growing. A partial list of these organisms includes: *Staphylococcus* spp., such as *S. aureus*; *Enterococcus* spp., such as *E. faecalis*; *Pseudomonas* spp., such as *P. aeruginosa*, *Clostridium* spp., such as *C. botulinum*, *Haemophilus* spp., such as *H. influenzae*; *Enterobacter* spp., such as *E. cloacae*, *Vibrio* spp., such as *V. cholera*; *Moraxala* spp., such as *M. catarrhalis*; *Streptococcus* spp., such as *S. pneumoniae*, *Neisseria* spp., such as *N. gonorrhoeae*; *Mycoplasma* spp., such as *Mycoplasma pneumoniae*; *Salmonella typhimurium*; *Helicobacter pylori*; *Escherichia coli*; and *Mycobacterium tuberculosis*. The sequences identified as required for proliferation in the present invention can be used to probe these and other organisms to identify homologous required proliferation genes contained therein.

In one embodiment of the present invention, the nucleic acid sequences disclosed herein are used to screen genomic libraries generated from bacterial species of interest other than *E. coli*. For example, the genomic library may be from *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium*



*tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. Standard molecular biology techniques are used to generate genomic libraries from various microorganisms. In one aspect, the libraries are generated and bound to nitrocellulose paper. The identified exogenous nucleic acid sequences of the present invention can then be used as probes to screen the libraries for homologous sequences. The homologous sequences identified can then be used as targets for the identification of new, antimicrobial compounds with activity against more than one organism.

For example, the preceding methods may be used to isolate nucleic acids having a sequence with at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% identity to a nucleic acid sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 1-81, 405-485, 82-88, 90-242, fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto. Identity may be measured using BLASTN version 2.0 with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, *Nucleic Acid Res.* 25: 3389-3402 (1997), the disclosure of which is incorporated herein by reference in its entirety). For example, the homologous polynucleotides may have a coding sequence which is a naturally occurring allelic variant of one of the coding sequences described herein. Such allelic variants may have a substitution, deletion or addition of one or more nucleotides when compared to the nucleic acids of SEQ ID NOS: 1-81, 405-485, 82-88, 90-242 or the sequences complementary thereto.

Additionally, the above procedures may be used to isolate nucleic acids which encode polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, or at least 40% identity or similarity to a polypeptide having the sequence of one of SEQ ID NOS: 243-357, 359-398 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.0t78 algorithm with the default parameters. Alternatively, protein identity or similarity may be identified using BLASTP with the default parameters, BLASTX with the default parameters, or TBLASTN with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, *Nucleic Acid Res.* 25: 3389-3402 (1997), the disclosure of which is incorporated herein by reference in its entirety).

Alternatively, homologous nucleic acids or polypeptides may be identified by searching a database to identify sequences having a desired level of homology to a nucleic acid or polypeptide involved in proliferation or an antisense nucleic acid to a nucleic acid involved in microbial proliferation. A variety of such databases are available to those skilled in the art, including GenBank and GenSeq. In some embodiments, the databases are screened to identify nucleic acids or polypeptides having at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, or at least 50%, at least 40% identity or similarity to a nucleic acid or polypeptide involved in proliferation or an antisense nucleic acid involved in proliferation. For example, the database may be screened to identify nucleic acids homologous to one of SEQ ID Nos. 1-81, 405-485, 82-88, 90-242 or polypeptides homologous

to SEQ ID NOs. 243-337, 359-398. In some embodiments, the database may be screened to identify homologous nucleic acids or polypeptides from organisms other than *E. coli*, including organisms such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

In another embodiment, gene expression arrays and microarrays can be employed. Gene expression arrays are high density arrays of DNA samples deposited at specific locations on a glass chip, nylon membrane, or the like. Such arrays can be used by researchers to quantify relative gene expression under different conditions. Gene expression arrays are used by researchers to help identify optimal drug targets, profile new compounds, and determine disease pathways. An example of this technology is found in U.S. Patent No. 5807522, which is hereby incorporated by reference.

It is possible to study the expression of all genes in the genome of a particular microbial organism using a single array. For example, the arrays from Genosys consist of 12 x 24 cm nylon filters containing PCR products corresponding to 4290 ORFs from *E. coli*. 10 ngs of each are spotted every 1.5 mm on the filter. Single stranded labeled cDNAs are prepared for hybridization to the array (no second strand synthesis or amplification step is done) and placed in contact with the filter. Thus the labeled cDNAs are of "antisense" orientation. Quantitative analysis is done by phosphorimager.

Hybridization of cDNA made from a sample of total cell mRNA to such an array followed by detection of binding by one or more of various techniques known to those in the art results in a signal at each location on the array to which cDNA hybridized. The intensity of the hybridization signal obtained at each location in the array thus reflects the amount of mRNA for that specific gene that was present in the sample. Comparing the results obtained for mRNA isolated from cells grown under different conditions thus allows for a comparison of the relative amount of expression of each individual gene during growth under the different conditions.

Gene expression arrays may be used to analyze the total mRNA expression pattern at various time points after induction of an antisense nucleic acid against a proliferation-required gene. Analysis of the expression pattern indicated by hybridization to the array provides information on whether or not the target gene of the antisense nucleic acid is being affected by antisense induction, how quickly the antisense is affecting the target gene, and for later timepoints, what other genes are affected by antisense expression. For example, if the antisense is directed against a gene for ribosomal protein L7/L12 in the 50S subunit, its targeted mRNA may disappear first and then other mRNAs may be observed to increase, decrease or stay the same. Similarly, if the antisense is directed against a different 50S subunit ribosomal protein mRNA (e.g. L25), that mRNA may disappear first followed by changes in mRNA expression that are similar to those seen with the L7/L12 antisense expression. Thus, the mRNA expression pattern observed

with an antisense nucleic acid against a proliferation required gene may identify other proliferation-required nucleic acids in the same pathway as the target of the antisense nucleic acid. In addition, the mRNA expression patterns observed with candidate drug compounds may be compared to those observed with antisense nucleic acids against a proliferation-required nucleic acid. If the mRNA expression pattern observed with the candidate drug compound is similar to that observed with the antisense nucleic acid, the drug compound may be a promising therapeutic candidate. Thus, the assay would be useful in assisting in the selection of candidate drug compounds for use in screening methods such as those described below.

In cases where the source of nucleic acid deposited on the array and the source of the nucleic acid being hybridized to the array are from two different organisms, gene expression arrays can identify homologous genes in the two organisms.

The present invention also contemplates additional methods for screening other microorganisms for proliferation-required genes. In this embodiment, the conserved portions of sequences identified as proliferation-required can be used to generate degenerate primers for use in the polymerase chain reaction (PCR). The PCR technique is well known in the art. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. This homologous gene is then isolated, expressed, and used as a target for candidate antibiotic compounds. In another aspect of this embodiment, the homologous gene is expressed in an autologous organism or in a heterologous organism in such a way as to alter the level or activity of a homologous gene required for proliferation in the autologous or heterologous organism. In still another aspect of this embodiment, the homologous gene or portion is expressed in an antisense orientation in such a way as to alter the level or activity of a nucleic acid required for proliferation of an autologous or heterologous organism.

The homologous sequences to proliferation-required genes identified using the techniques described herein may be used to identify proliferation-required genes of organisms other than *E. coli*; to inhibit the proliferation of organisms other than *E. coli* by inhibiting the activity or reducing the amount of the identified homologous nucleic acid or polypeptide in the organism other than *E. coli*, or to identify compounds which inhibit the growth of organisms other than *E. coli* as described below.

In another embodiment of the present invention, *E. coli* sequences identified as required for proliferation are transferred to expression vectors capable of function within non-*E. coli* species. As would be appreciated by one of ordinary skill in the art, expression vectors must contain certain elements that are species specific. These elements can include promoter sequences, operator sequences, repressor genes, origins of replication, ribosomal binding sequences, termination sequences, and others. To use the identified exogenous sequences of the present invention, one of ordinary skill in the art would know to use standard molecular biology techniques to isolate vectors containing the sequences of interest from cultured bacterial cells, isolate and purify those sequences, and subclone those sequences into an expression vector adapted for use in the species of bacteria to be screened.

Expression vectors for a variety of other species are known in the art. For example, Cao et al. report the expression of steroid receptor fragments in *Staphylococcus aureus*. J. Steroid Biochem Mol Biol. 44(1):1-11

(1993). Also, Pla et al. have reported an expression vector that is functional in a number of relevant hosts including: *Salmonella typhimurium*, *Pseudomonas putida*, and *Pseudomonas aeruginosa*. *J. Bacteriol.* 172(8):4448-55 (1990). These examples demonstrate the existence of molecular biology techniques capable of constructing expression vectors for the species of bacteria of interest to the present invention.

5        Following the subcloning of the identified nucleic acid sequences into an expression vector functional in the microorganism of interest, the identified nucleic acid sequences are conditionally transcribed to assay for bacterial growth inhibition. Those expression vectors found to contain sequences that, when transcribed, inhibit bacterial growth are compared to the known genomic sequence of the pathogenic microorganism being screened or, if the homologous sequence from the organism being screened is not known, it may be identified and isolated by  
10        hybridization to the proliferation-required *E. coli* sequence of interest or by amplification using primers based on the proliferation-required *E. coli* sequence of interest as described above.

      The antisense sequences from the second organism which are identified as described above may then be operably linked to a promoter, such as an inducible promoter, and introduced into the second organism. The techniques described herein for identifying *E. coli* genes required for proliferation may thus be employed to determine  
15        whether the identified sequences from a second organism inhibit the proliferation of the second organism.

      Antisense nucleic acids required for the proliferation of organisms other than *E. coli* or the genes corresponding thereto, may also be hybridized to a microarray containing the *E. coli* ORFs to gauge the homology between the *E. coli* sequences and the proliferation-required nucleic acids from other organisms. For example, the proliferation-required nucleic acid may be from *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni* or *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The proliferation-required nucleic acids from an organism other than *E. coli* may be hybridized to the array under a variety of conditions which permit hybridization to occur when the probe has different levels of homology to the sequence on the microarray. This would provide an indication of homology across the organisms as well as clues to other possible essential genes in these organisms.

30        In still another embodiment, the exogenous nucleic acid sequences of the present invention that are identified as required for bacterial growth or proliferation can be used as antisense therapeutics for killing bacteria. The antisense sequences can be directed against the proliferation-required genes whose sequence corresponds to the exogenous nucleic acid probes identified here (i.e. the antisense nucleic acid may hybridize to the gene or a portion thereof). Alternatively, antisense therapeutics can be directed against operons in which proliferation-required genes reside (i.e. the antisense  
35        nucleic acid may hybridize to any gene in the operon in which the proliferation-required genes reside). Further, antisense

therapeutics can be directed against a proliferation-required gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual sequence that is required for bacterial proliferation or an operon containing a proliferation-required gene.

In addition to therapeutic applications, the present invention encompasses the use of nucleic acid sequences complementary to sequences required for proliferation as diagnostic tools. For example, nucleic acid probes complementary to proliferation-required sequences that are specific for particular species of microorganisms can be used as probes to identify particular microorganism species in clinical specimens. This utility provides a rapid and dependable method by which to identify the causative agent or agents of a bacterial infection. This utility would provide clinicians the ability to prescribe species specific antimicrobial compounds to treat such infections. In an extension of this utility, antibodies generated against proteins translated from mRNA transcribed from proliferation-required sequences can also be used to screen for specific microorganisms that produce such proteins in a species-specific manner.

The following examples teach the genes of the present invention and a subset of uses for the *E. coli* genes identified as required for proliferation. These examples are illustrative only and are not intended to limit the scope of the present invention.

#### EXAMPLES

The following examples are directed to the identification and exploitation of *E. coli* genes required for proliferation. Methods of gene identification are discussed as well as a variety of methods to utilize the identified sequences.

#### **Genes Identified as Required for Proliferation of *E. coli***

Exogenous nucleic acid sequences were cloned into an inducible expression vector and assayed for growth inhibition activity. Example 1 describes the examination of a library of exogenous nucleic acid sequences cloned into IPTG-inducible expression vectors. Upon activation or induction, the expression vectors produced an RNA molecule corresponding to the subcloned exogenous nucleic acid sequences. The RNA product was in an antisense orientation with respect to the *E. coli* genes from which it was originally derived. This antisense RNA then interacted with sense mRNA produced from various *E. coli* genes and interfered with or inhibited the translation of the sense messenger RNA (mRNA) thus preventing protein production from these sense mRNA molecules. In cases where the sense mRNA encoded a protein required for the proliferation, bacterial cells containing an activated expression vector failed to grow or grew at a substantially reduced rate.

#### **EXAMPLE 1**

##### Inhibition of Bacterial Proliferation after IPTG induction

To study the effects of transcriptional induction in liquid medium, growth curves were carried out by back diluting cultures 1:200 into fresh media with or without 1 mM IPTG and measuring the OD<sub>450</sub> every 30 minutes (min). To

study the effects of transcriptional induction on solid medium,  $10^2$ ,  $10^3$ ,  $10^4$ ,  $10^5$ ,  $10^6$ ,  $10^7$  and  $10^8$  fold dilutions of overnight cultures were prepared. Aliquots of from 0.5 to 3  $\mu$ l of these dilutions were spotted on selective agar plates with or without 1 mM IPTG. After overnight incubation, the plates were compared to assess the sensitivity of the clones to IPTG.

Of the numerous clones tested, some clones were identified as a containing sequence that inhibited *E. coli* growth after IPTG induction. Accordingly, the gene to which the inserted nucleic acid sequence corresponds, or a gene within the operon containing the inserted nucleic acid, may be required for proliferation in *E. coli*.

#### Characterization of Isolated Clones Negatively Affecting *E. coli* Proliferation

Following the identification of those expression vectors that, upon expression, negatively impacted *E. coli* growth or proliferation, the inserts or nucleic acid fragments contained in those expression vectors were isolated for subsequent characterization. Expression vectors of interest were subjected to nucleic acid sequence determination.

#### EXAMPLE 2

##### Nucleic Acid Sequence Determination of Identified Clones Expressing Nucleic Acid Fragments with Detrimental Effects of *E. coli* Proliferation

The nucleotide sequences for the exogenous identified sequences were determined using plasmid DNA isolated using QIAPREP (Qiagen, Valencia, CA) and methods supplied by the manufacturer. The primers used for sequencing the inserts were 5' - TGTTTATCAGACCGCTT - 3' (SEQ ID NO: 403) and 5' - ACAATTTACACAGCCTC - 3' (SEQ ID NO: 404). These sequences flank the polylinker in pLEX5BA. Sequence identification numbers (SEQ ID NOs) for the identified inserts are listed in Table I and discussed below.

#### EXAMPLE 3

##### Comparison Of Isolated Sequences to Known Sequences

The nucleic acid sequences of the subcloned fragments obtained from the expression vectors discussed above were compared to known *E. coli* sequences in GenBank using BLAST version 1.4 or version 2.0.6 using the following default parameters: Filtering off, cost to open a gap=5, cost to extend a gap=2, penalty for a mismatch in the blast portion of run=-3, reward for a match in the blast portion of run=1, expectation value (e)=10.0, word size=11, number of one-line descriptions=100, number of alignments to show (B)=100. BLAST is described in Altschul, J Mol Biol. 215:403-10 (1990), the disclosure of which is incorporated herein by reference in its entirety. Expression vectors were found to contain nucleic acid sequences in both the sense and antisense orientations. The presence of known genes, open reading frames, and ribosome binding sites was determined by comparison to public databases holding genetic information and various computer programs such as the Genetics Computer Group programs FRAMES and CODONPREFERENCE. Clones were designated as "antisense" if the cloned fragment was oriented to the promoter such that the RNA transcript produced was complementary to the expressed mRNA from a chromosomal locus. Clones were designated as "sense" if they coded for an RNA fragment that was identical to a portion of a wild type mRNA from a chromosomal locus.

The sequences described in Examples 1-2 that inhibited bacterial proliferation and contained gene fragments in an antisense orientation are listed in Table I. This table lists each identified sequence by: a sequence identification number; a Molecule Number; a gene to which the identified sequence corresponds, listed according to the National Center for Biotechnology Information (NCBI), Blattner (Science 277:1453-1474(1997); also contains the *E. coli* K-12 genome sequence), or Rudd (Micro. and Mol. Rev. 62:985-1019 (1998)), (both papers are hereby incorporated by reference) nomenclatures. The CONTIG numbers for each identified sequence is shown, as well as the location of the first and last base pairs located on the *E. coli* chromosome. A Molecule Number with a "\*\*\*" indicates a clone corresponding to an intergenic sequence.

The sequences of the nucleic acid inserts of SEQ ID NOs: 1-81 from U.S. Provisional Patent Application No. 60/117,405 which inhibited proliferation were further analyzed. The reanalyzed sequences corresponding to SEQ ID NOs. 1-81 of U.S. Provisional Patent Application No. 60/117,405 have SEQ ID NOs. 405-485 in the present application.

SEQ ID NOs: 82-242 in U.S. Provisional Patent Application No. 60/117,405 are identical to SEQ ID NOs: 82-242 of the present application with the following exceptions. SEQ ID NO: 148 in the present application is the complementary strand of SEQ ID NO: 148 in U.S. Provisional Patent Application No. 60/117,405. Accordingly, the protein of SEQ ID NO: 308 which is encoded by SEQ ID NO: 148 has also been revised. SEQ ID NO: 163 in the present application is the complementary strand of SEQ ID NO: 163 in U.S. Provisional Patent Application No. 60/117,405. Accordingly, the protein of SEQ ID NO: 323 which is encoded by SEQ ID NO: 163 has also been revised.

The target gene of SEQ ID NOs. 18 and 19 of U.S. Provisional Patent Application No. 60/117,405 (SEQ ID NOs. 18, 19, 422, 423 of the present application) has been revised from *dicF* to *ftsZ* to reflect the fact that these SEQ ID NOs. include natural antisense molecules which inhibit *ftsZ* expression.

The gene products of the nucleic acids of SEQ ID NOs. 198 and 239-242 in U.S. Provisional Patent Application No. 60/117,405 and in the present application (SEQ ID NOs. 358 and 399-402 of the present application) have been revised to reflect the fact that these nucleic acids encode nontranslated tRNAs and rRNAs. Tables I and II have been revised accordingly. The SEQ ID NOs. in Table II were also revised to reflect the fact that SEQ ID NOs: 89 and 402 were identical in U.S. Provisional Patent Application No. 60/117,405.

TABLE I

Identified Clones with Corresponding Genes and Operons

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
1, 405	EcXA001	<i>yhhQ</i>	<i>b3471</i>	<i>yhhQ</i>	AE000423
2, 406	EcXA002	<i>lepB</i>	<i>lepB</i>	<i>lepB</i>	AE000343
3, 407	EcXA003	<i>f586</i>	<i>b0955</i>	<i>ycbZ</i>	AE000197
4, 408	EcXA004	<i>rpsG, rpsL</i>	<i>b3341</i>	<i>rpsG, rpsL</i>	AE000410
5, 409	EcXA005a	<i>rplL, rplJ</i>	<i>b3986</i>	<i>rplL, rplJ</i>	AE000472
6, 410	EcXA005b	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
7, 411	EcXA005c	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	AE000472
8, 412	EcXA005d	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	AE000472
9, 413	EcXA005e	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
10, 414	EcXA005f	<i>rpIL</i>	<i>rpIL</i>	<i>rpIL</i>	AE000472
11, 415	EcXA005g	<i>rpIL</i>	<i>rpIL</i>	<i>rpIL</i>	AE000472
12, 416	EcXA006	<i>pta</i>	<i>b2297</i>	<i>pta</i>	AE000319
13, 417	EcXA007	<i>yicP</i>	<i>b3666</i>	<i>yicP</i>	AE000444
14, 418	EcXA008a	<i>yhaU</i>	<i>b3127</i>	<i>yhaU</i>	AE000394
15, 419	EcXA008b	<i>yhaU</i>	<i>yhaU</i>	<i>yhaU</i>	AE000394
16, 420	EcXA008c	<i>yhaU</i>	<i>yhaU</i>	<i>yhaU</i>	AE000394
17, 421	EcXA009	<i>ydeY</i>	<i>ydeY</i>	<i>ydeY</i>	AE000249
18, 422	EcXA010a (natural as)	<i>dicF</i>	<i>b1575</i>	<i>dicF</i>	AE000253
19, 423	EcXA010b	<i>dicF</i>	<i>dicF</i>	<i>dicF</i>	AE000253
20, 424	EcXA011	<i>fdnG</i>	<i>b1474</i>	<i>fdnG</i>	AE000244
21, 425	EcXA012a	<i>fusA</i>	<i>b3340</i>	<i>fusA</i>	AE000410
22, 426	EcXA012b	<i>fusA</i>	<i>fusA</i>	<i>fusA</i>	AE000410
23, 427	EcXA012c	<i>fusA</i>	<i>fusA</i>	<i>fusA</i>	AE000410
24, 428	EcXA013a	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
25, 429	EcXA013b	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
26, 430	EcXA013c	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
27, 431	EcXA014	<i>visC</i>	<i>b2906</i>	<i>visC</i>	AE000374
28, 432	EcXA015	<i>yfdI</i>	<i>yfdI</i>	<i>yfdI</i>	AE000323
29, 433	EcXA016	<i>yeaQ</i>	<i>yeaQ</i>	<i>yeaQ</i>	AE000274
		<i>yoaG</i>	<i>yoaG</i>	<i>yoaG</i>	
30, 434	EcXA017a	<i>yggE</i>	<i>b2922</i>	<i>yggE</i>	AE000375
31, 435	EcXA017b	<i>yggE</i>	<i>yggE</i>	<i>yggE</i>	AE000375
32, 436	EcXA018a	<i>o464</i>	<i>b2074</i>	<i>yegM</i>	AE000297
33, 437	EcXA018b	<i>o464</i>	<i>b2074</i>	<i>yegM</i>	AE000297
34, 438	EcXA019a	<i>yehA</i>	<i>yehA</i>	<i>yehA</i>	AE000300
					AE000299
35, 439	EcXA019b	<i>o172, yehA</i>	<i>o172, yehA</i>	<i>o172, yehA</i>	AE000299
36, 440	EcXA020	<i>o384, f82</i>	<i>b1794, b1795</i>	<i>yeaP, yeaQ</i>	AE000274
37, 441	EcXA021a	<i>f112</i>	<i>b0218</i>	<i>yafU</i>	AE000130
38, 442	EcXA021b	<i>f112</i>	<i>b0218</i>	<i>yafU</i>	AE000130
39, 443	EcXA022	<i>o740</i>	<i>b1629</i>	<i>ydgN</i>	AE000258
40, 444	EcXA023a	<i>f176, f382</i>	<i>b1504, b1505</i>	<i>ydeS, ydeT</i>	AE000247
41, 445	EcXA023b	<i>f176, f382</i>	<i>b1504, b1505</i>	<i>ydeS, ydeT</i>	AE000247
42, 446	EcXA024	<i>ygiM, ygiN</i>	<i>b3082</i>	<i>ygiM, ygiN</i>	AE000390
43, 447	EcXA025	<i>O2383</i>	<i>b1878</i>	<i>yeaJ</i>	AE000289
44, 448	EcXA026	<i>o61</i>	<i>Unpre-dicted</i>	<i>Unpre-dicted</i>	AE000138
45, 449	EcXA027a	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
46, 450	EcXA027b	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
47, 451	EcXA027c	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
		<i>yohI</i>	<i>yohI</i>	<i>yohI</i>	
48, 452	EcXA027d	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
49, 453	EcXA028	<i>f296</i>	<i>b2305</i>	<i>yfcI</i>	AE000319
50, 454	EcXA029	<i>yjiK</i>	<i>b4391</i>	<i>yjiK</i>	AE000509
51, 455	EcXA030	<i>yi5A</i>	<i>b3557</i>	<i>yi5A</i>	AE000433
52, 456	EcXA031	<i>rplE</i>	<i>B3308</i>	<i>rplE</i>	AE000408
53, 457	EcXA032a	<i>ybgD</i>	<i>ybgD</i>	<i>ybgD</i>	AE000175
54, 458	EcXA032b**	<i>ybgD</i>	<i>ybgD</i>	<i>ybgD</i>	AE000175



SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
		<i>gltA</i>	<i>gltA</i>	<i>gltA</i>	
55, 459	EcXA033a	<i>f477 (as)</i>	<i>b3052</i>	<i>waaE</i>	AE000387
					AE000386
56, 460	EcXA033b	<i>f477</i>	<i>b3052</i>	<i>waaE</i>	AE000387
57, 461	EcXA034a	<i>cspA</i>	<i>b3556</i>	<i>cspA</i>	AE000433
58, 462	EcXA034b	<i>cspA</i>	<i>b3556</i>	<i>cspA</i>	AE000433
59, 463	EcXA035	<i>yhjU</i>	<i>yhjU</i>	<i>yhjU</i>	AE000431
60, 464	EcXA036	<i>yqjF</i>	<i>b3101</i>	<i>yqjF</i>	AE000392
		<i>o99</i>	<i>b3100</i>	<i>yqjK</i>	
61, 465	EcXA037	<i>ydeH</i>	<i>b1535</i>	<i>ydeH</i>	AE000251
62, 466	EcXA038	<i>sieB</i>	<i>b1353</i>	<i>sieB</i>	AE000233
63, 467	EcXA039	<i>ybbD</i>		<i>ybbD</i>	AE000156
64, 468	EcXA040	<i>insB 6</i>	<i>b3445</i>	<i>insB 6</i>	AE000420
65, 469	EcXA041	<i>f234</i>	<i>b1138</i>	<i>ymfE</i>	AE000214
66, 470	EcXA042a	<i>rplY</i>	<i>rplY</i>	<i>rplY</i>	AE000308
67, 471	EcXA042b	<i>rplY</i>	<i>rplY</i>	<i>rplY</i>	AE000308
68, 472	EcXA043	<i>ybgB</i>	<i>ybgB</i>	<i>ybgB</i>	AE000176
		<i>cydA</i>	<i>cydA</i>	<i>cydA</i>	
69, 473	EcXA044	<i>purB</i>	<i>b1131</i>	<i>purB</i>	AE000213
70, 474	EcXA045**	<i>csrA</i>	<i>csrA</i>	<i>csrA</i>	AE000353
		<i>serV</i>	<i>serV</i>	<i>serV</i>	
71, 475	EcXA046**	<i>fimE, fimA</i>	<i>b4313</i>	<i>fimE, fimA</i>	AE000502
72, 476	EcXA047**	<i>f96, cspB</i>	<i>f96, cspB</i>	<i>cspB, ydtS</i>	AE000252
73, 477	EcXA048	<i>yefE</i>	<i>yefE</i>	<i>yefE</i>	AE000294
74, 478	EcXA049	<i>yaiC</i>	<i>b0385</i>	<i>yaiC</i>	AE000145
75, 479	EcXA050	<i>o467, o222</i>	<i>yaiU, yaiV</i>	<i>yaiU, yaiV</i>	AE000144
76, 480	EcXA051a	<i>rplB, rplW</i>	<i>rplB, rplW</i>	<i>rplB, rplW</i>	AE000408
77, 481	EcXA051b	<i>rplW</i>	<i>rplW</i>	<i>rplW</i>	AE000408
78, 482	EcXA052	<i>infC</i>	<i>infC</i>	<i>infC</i>	AE000267
					AE000266
79, 483	EcXA053	<i>gor</i>	<i>gor</i>	<i>gor</i>	AE000426
80, 484	EcXA054	<i>rplF</i>	<i>rplF</i>	<i>rplF</i>	AE000408
81, 485	EcXA055	<i>rrlG</i>	<i>rrlG</i>	<i>rrlG</i>	AE000345

## EXAMPLE 4

Identification of Genes and their Corresponding Operons Affected by Antisense Inhibition

The sequencing of the entire *E. coli* genome is described in Blattner et al., Science 277:1453-1474(1997) the entirety of which is hereby incorporated by reference and the sequence of the genome is listed in GenBank Accession No.U00096, the disclosure of which is incorporated herein by reference in its entirety. The operons to which the proliferation-inhibiting nucleic acids correspond were identified using RegulonDB and information in the literature. The coordinates of the boundaries of these operons on the *E. coli* genome are listed in Table III. Table II lists the molecule numbers of the inserts containing the growth inhibiting nucleic acid fragments, the genes in the operons corresponding to the inserts, the SEQ ID NOs of the genes containing the inserts, the SEQ ID NOs of the proteins encoded by the genes, the start and stop points of the genes on the *E. coli* genome, the orientation of the genes on the genome, whether the operons

are predicted or documented, and the predicted functions of the genes. The identified operons, their putative functions, and whether or not the genes are presently thought to be required for proliferation are discussed below.

5 Functions for the identified genes were determined by using either Blattner functional class designations or by comparing identified sequence with known sequences in various databases. A variety of biological functions were noted for the genes to which the clones of the present invention correspond. The functions for the genes of interest appear in Table II.

The proteins that are listed in Table II are involved in a wide range of biological functions.

**TABLE II**  
All Operon Data with Whole Chromosome Coordinates

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
82	243	EcXA001	<i>yhhQ</i>	3606848	3607513	(P)	Hypothetical ORF, unclassified, unknown	Hypothetical outer membrane protein
83	244		<i>dcrB</i>	3607532	3608143		Hypothetical ORF, unclassified, unknown	Resistance to phage C1; periplasmic protein perhaps anchored to inner membrane
84	245	EcXA002	<i>lepB</i>	2702355	2703329	(P)	Transport and binding proteins	Secretion
85	246	EcXA003	<i>ycbZ</i>	1015762	1017522	(P)	Unknown	Protease
86	247	EcXA004	<i>tulA</i>	3467782	3468966	(D)	Translation, post-translational modification	Translation (Elongation factor Tu)
87	248		<i>fusA</i>	3469037	3471151		Translation, post-translational modification	Translation (elongation factor elfg)
88	249		<i>rpsG</i>	3471179	3471718		Translation, post-translational modification	Translation
89	402	EcXA055	<i>rrsG</i>	2727636	2729178		Translation, post-translational modification	Translation (rRNA)
90	250		<i>rpsL</i>	3471815	3471815		Translation, post-translational modification	Translation
91	251	EcXA005a-g	<i>rplJ</i>	4177574	4178071	(D)	Translation, post-translational modification	Translation
92	252		<i>rplL</i>	4178138	4178503		Translation, post-translational modification	Translation
93	253	EcXA006	<i>pta</i>	2412767	2414911	(P)	Carbon compound catabolism	Carbon compound catabolism
94	254	EcXA007	<i>yicP</i>	3841591	3843357	(P)	Hypothetical ORF, unclassified, unknown	Probable adenine deaminase

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
95	255	EcXA008a-c	<i>yhaD</i>	3288266	3269492	(P)	Hypothetical ORF, unclassified, unknown	
96	256		<i>yhaE</i>	3269508	3270407		Putative enzymes	
97	257		<i>yhaF</i>	3270428	3271198		Hypothetical ORF, unclassified, unknown	
98	258		<i>yhaU</i>	3271214	3272548		Carbon compound catabolism	Probable integral membrane protein Phthalate permease family
99	259	EcXA009	<i>ydeX</i>	1599514	1601049	(P)	Putative transport proteins	
100	260		<i>ydeY</i>	1601043	1602071		Putative transport proteins	Putative ABC transporter
101	261		<i>ydeZ</i>	1602071	1603063		Hypothetical ORF, unclassified, unknown	
102	262		<i>yneA</i>	1603075	1604097		Hypothetical ORF, unclassified, unknown	
103	263		<i>yneB</i>	1604124	1604999		Hypothetical ORF, unclassified, unknown	
104	264		<i>yneC</i>	1605023	1605313		Hypothetical ORF, unclassified, unknown	
105	265	EcXA010a-b	<i>ftsZ</i>	105305	106456	(P)	Cell processes (incl. Adaptation, protection)	Regulator of cell division
106	266	EcXA011	<i>fdnG</i>	1545425	1548472	(D)	Energy metabolism	Anaerobic respiration (formate dehydrogenase)
107	267		<i>fdnH</i>	1548485	1549369		Energy metabolism	
108	268		<i>fdnI</i>	1549362	1550015		Energy metabolism	
		EcXA 012a-c	Same operon as EcXA004					
109	269	EcXA013a-c	<i>yhlL</i>	2697683	2697943	(P)	Hypothetical ORF, unclassified, unknown	No homologues, no motifs
110	270	EcXA014	<i>visC</i>	3049135	3050337	(P)	Hypothetical ORF, unclassified, unknown	Ubiquinone synthesis

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
111	271		<i>ubiH</i>	3050360	3051538		Biosynthesis of cofactors, prosthetic groups and carriers	
112	272		<i>pepP</i>	3051535	3052860		Translation, post-translational modification	
113	273		<i>ygIB</i>	3052886	3053470		Hypothetical ORF, unclassified, unknown	
114	274	EcXA015	<i>yfdG</i>	2465875	2466237	(P)	Hypothetical ORF, unclassified, unknown	
115	275		<i>yfdH</i>	2466234	2467154		Cell structure	Putative membrane protein
116	276		<i>yfdI</i>	2467151	2468482		Hypothetical ORF, unclassified, unknown	
117	277	EcXA016	<i>yeaQ</i>	1877031	1877279	(P)	Hypothetical ORF, unclassified, unknown	Homologue to transglycosylase associated protein
118	278		<i>yeaG</i>	1877427	1877609	(P)	Hypothetical ORF, unclassified, unknown	No homologues
119	279		<i>yeaR</i>	1877613	1877972		Hypothetical ORF, unclassified, unknown	
120	280	EcXA017a-b	<i>yggE</i>	3065360	3066100	(P)	Structural proteins	Homologues in multiple bacteria, no motifs
121	281	EcXA018a-b	<i>yegM</i>	2151891	2153285	(P)	Putative transport proteins	Transport (multiple transferable resistance)
122	282		<i>yegN</i>	2153285	2156407		Hypothetical ORF, unclassified, unknown	
123	283		<i>yegO</i>	2156408	2159485		Hypothetical ORF, unclassified, unknown	
124	284		<i>yegB</i>	2159486	2160901		Putative transport proteins	
125	285	EcXA019a-b	<i>yehA</i>	2185400	2186434	(P)	Cell structure	Weak homology to pilin precursor from <i>H. Inf.</i>

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
126	286		<i>yehB</i>	2186450	2186930		Hypothetical ORF, unclassified, unknown	
127	287		<i>yehC</i>	2188946	2189665		Putative chaperones	
128	288		<i>yehD</i>	2189700	2190242		Cell structure	
		EcXA020	Same operon as EcXA016 (one of the two)					
129	289	EcXA021a-b	<i>yafU</i>	238746	239084	(P)	Hypothetical ORF, unclassified, unknown	Homologues in <i>H. Inf.</i> and <i>S. Pombe.</i> , no motifs, transmembrane region present
130	290	EcXA022	<i>ydgL</i>	1703791	1704372	(P)	Hypothetical ORF, unclassified, unknown	
131	291		<i>ydgM</i>	1704372	1704950		Hypothetical ORF, unclassified, unknown	
132	292		<i>ydgN</i>	1704943	1707165		Hypothetical ORF, unclassified, unknown	
133	293		<i>ydgO</i>	1707166	1708224		Hypothetical ORF, unclassified, unknown	
134	294		<i>ydgP</i>	1708228	1708848		Hypothetical ORF, unclassified, unknown	
135	295		<i>ydgQ</i>	1708852	1709547		Hypothetical ORF, unclassified, unknown	
136	296		<i>nth</i>	1709547	1710182		Transcription, RNA processing and degradation	
137	297	EcXA023a-b	<i>ydeR</i>	1585817	1586320	(P)	Hypothetical ORF, unclassified, unknown	
138	298		<i>ydeS</i>	1586333	1586863		Hypothetical ORF, unclassified, unknown	fimf-like

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
139	299		<i>ydeT</i>	1586877	1588025		Structural proteins	fimL-like
140	300	EcXA024	<i>ygjM</i>	3231369	3231785	(P)	Hypothetical ORF, unclassified, unknown	Weak homology to long chain fatty acid coa ligase in <i>Archaeoglobus</i>
141	301		<i>ygjN</i>	3231782	3232096		Hypothetical ORF, unclassified, unknown	Homologues in various bacteria
142	302	EcXA025	<i>yeeJ</i>	2042885	2050036	(P)	Hypothetical ORF, unclassified, unknown	Strong similarity to numerous attaching and effacing proteins and invasins
143	303	EcXA026	<i>rajA</i>	331001	331184	unpredicted		nifm-like
144	304	EcXA027a-d	<i>yohG</i>	2225343	2226539	(P)	Putative transport proteins	
145	305		<i>yohH</i>	2226569	2226859		Hypothetical ORF, unclassified, unknown	Xylose binding protein-like
146	306		<i>yohI</i>	2227458	2228405	(P)	Putative regulatory protein	
147	307	EcXA028	<i>ycfI</i>	2420669	2421559	(P)	Hypothetical ORF, unclassified, unknown	Similar to <i>S. Typhi</i> histidine transport gene
148	308	EcXA029	<i>yjJK</i>	4626424	4628091	(P)	Hypothetical ORF, unclassified, unknown	Similar to ABC transporter
149	309	EcXA030	<i>yj5A</i>	3718309	3718830	(P)	Hypothetical ORF, unclassified, unknown	IS150 orf A
150	310		<i>yj5B</i>	3718827	3719678		Phage, transposon, or plasmid	
151	311	EcXA031	<i>rpmJ</i>	3440255	3440371	(D)	Translation, post-translational modification	
152	312		<i>prlA</i>	3440403	3441734		Putative transport proteins	
153	313		<i>rplO</i>	3441742	3442176		Translation, post-translational modification	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
154	314		<i>rpmD</i>	3442180	3442359		Translation, post-translational modification	
155	315		<i>rpsE</i>	3442363	3442866		Translation, post-translational modification	
156	316		<i>rplR</i>	3442881	3443234		Translation, post-translational modification	
157	317		<i>rplF</i>	3443244	3443777		Translation, post-translational modification	Translation
158	318		<i>rpsH</i>	3443790	3444182		Translation, post-translational modification	
159	319		<i>rpsN</i>	3444216	3444521		Translation, post-translational modification	
160	320		<i>rplE</i>	3444536	3445075		Translation, post-translational modification	Translation
161	321		<i>rplX</i>	3445090	3445404		Translation, post-translational modification	
162	322		<i>rplN</i>	3445415	3445786		Translation, post-translational modification	
163	323	EcXA032a-b	<i>ybgD</i>	751452	752018	(P)	Cell processes (incl. Adaptation, protection)	Hypothetical fimbrial protein
164	324		<i>gltA</i>	752408	753691	(D)	Energy metabolism	Glutamine biosynthesis
165	325	EcXA033a-b	<i>waaE</i>	3192961	3194394	(P)	Putative enzymes	ADP heptose synthase/ autotrophic growth protein
166	326		<i>glnE</i>	3194442	3197282		Translation, post-translational modification	
167	327		<i>ygiF</i>	3197305	3198606		Hypothetical ORF, unclassified, unknown	
168	328	EcXA034a-b	<i>cspA</i>	3717678	3717890	(P)	Cell processes (incl. Adaptation, protection)	RNA chaperonin
169	329	EcXA035	<i>yjiS</i>	3694087	3695658	(P)	Translation, post-translational modification	



GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
170	330		<i>yhjT</i>	3695658	3695846		Hypothetical ORF, unclassified, unknown	
171	331		<i>yhjU</i>	3695843	3697522		Hypothetical ORF, unclassified, unknown	Regions similar to dehydrogenases, nucleases etc.
172	332	EcXA036	<i>yqiC</i>	3246594	3246977	(P)	Hypothetical ORF, unclassified, unknown	
173	333		<i>yqiD</i>	3247015	3247320		Hypothetical ORF, unclassified, unknown	
174	334		<i>yqiE</i>	3247323	3247727		Hypothetical ORF, unclassified, unknown	
175	335		<i>yqiK</i>	3247717	3248016		Similar to mukB from H. Inf.	
176	336		<i>yqiF</i>	3248112	3248594	(P)	Hypothetical ORF, unclassified, unknown	Homologues in many bacteria, blocks; secretion/ ATP synthase/ftsZ
177	337	EcXA037	<i>ydeH</i>	1620984	1621874	(P)	Hypothetical ORF, unclassified, unknown	Similar to carboxy-kinase, oxidase, symporters
178	338	EcXA038	<i>sieB</i>	1416572	1417183	(P)	Phage, transposon, or plasmid	Super-infection exclusion factor B-like
179	339		<i>rajB (b135d)</i>	1417192	1417368		Hypothetical ORF, unclassified, unknown	
180	340	EcXA039	<i>rhsD</i>	522485	526765	(P)	Hypothetical ORF, unclassified, unknown	
181	341		<i>ybbC</i>	526805	527173		Hypothetical ORF, unclassified, unknown	
182	342		<i>ybbH</i>	527173	527683		Hypothetical ORF, unclassified, unknown	Rhs-like element
183	343		<i>ybbD</i>	527864	528124		Hypothetical ORF, unclassified, unknown	ATP synthase, desaturase

GeneSeq ID No.	Gene Prod. Seq-ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
184	344		<i>yblI</i>	528163	528354		Hypothetical ORF, unclassified, unknown	
185	345	EcXA040	<i>insB_6</i>	351114	351389	(P)	Phage, transposon, or plasmid	
186	346		<i>insA</i>	351308	3581811		Phage, transposon, or plasmid	
187	347		<i>yrbA</i>	3580669	3581085		Hypothetical ORF, unclassified, unknown	
188	348		<i>yhbZ</i>	3579494	3580672		Hypothetical ORF, unclassified, unknown	
189	349	EcXA041	<i>ymfD</i>	1196090	1196755	(P)	Hypothetical ORF, unclassified, unknown	No assigned role
190	350		<i>ymfE</i>	1196756	1197460		Hypothetical ORF, unclassified, unknown	No assigned role
191	351	EcXA042a-b	<i>rplY</i>	2280537	2280821	(P)	Translation, post-translational modification	Translation
192	352	EcXA043	<i>hrsA</i>	765207	767183	(P)	Translation, post-translational modification	
193	353		<i>ybgB</i>	767201	769834		Carbon compound catabolism	Unknown
194	354		<i>cydA</i>	770678	772249	(D)	Energy metabolism	Cytochrome D oxidase
195	355		<i>cydB</i>	772265	773404		Energy metabolism	
196	356	EcXA044	<i>purB</i>	1189839	1191209	(D)	Nucleotide biosynthesis and metabolism	Purine biosynthesis
197	357	EcXA045	<i>csrA</i>	2816983	2817168	(P)	Regulatory function	Carbon storage regulator (mRNA decay factor)
198	358		<i>serV</i>	2816575	2816667	Unpredicted	Translation, post-translational modification	Translation (tRNA)
199	359	EcXA046	<i>fimB</i>	4538525	4539127	(D)	Cell structure	
200	360		<i>fimE</i>	4539605	4540201		Cell structure	Fimbriae
201	361		<i>fimA</i>	4540683	4541231		Cell structure	Regulator of inversion

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D)	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
202	362		<i>fimI</i>	4541188	4541835	Operon	Cell structure	
203	363		<i>fimC</i>	4541872	4542597		Cell structure	
204	364		<i>fimD</i>	4542665	4545301		Cell structure	
205	365		<i>fimF</i>	4545311	4545841		Cell structure	
206	366		<i>fimG</i>	4545854	4546357		Cell structure	
207	367		<i>fimH</i>	4546377	4547279		Cell structure	
208	368	EcXA047	<i>ydfP</i>	1637054	1638684	(P)	Hypothetical ORF, unclassified, unknown	
209	369		<i>ydfQ</i>	1637548	1638081		Hypothetical ORF, unclassified, unknown	
210	370		<i>ydfR</i>	1638078	1638389		Hypothetical ORF, unclassified, unknown	
211	371		<i>ydfS</i>	1638394	1638684		Hypothetical ORF, unclassified, unknown	Lysis protein
212	372		<i>csxB</i>	1639363	1639578	(P)	Cell processes (incl. Adaptation, protection)	
213	373	EcXA048	<i>yis2_7</i>	2099917	2100933	(P)	Phage, transposon, or plasmid	
214	374		<i>yefJ</i>	2100938	2101411		Putative enzymes	
215	375		<i>yefI</i>	2101413	2102531		Hypothetical ORF, unclassified, unknown	
216	376		<i>yefH</i>	2102516	2103106		Putative enzymes	
217	377		<i>yefG</i>	2103087	2104079		Hypothetical ORF, unclassified, unknown	
218	378		<i>rhc</i>	2104082	2105248		Cell structure	
219	379		<i>yefE</i>	2105248	2106351		Hypothetical ORF, unclassified, unknown	UDP galacto-pyranase mutase
220	380	EcXA049	<i>yaiC</i>	402927	404042	(P)	Hypothetical ORF, unclassified, unknown	Unknown
221	381	EcXA050	<i>yaiU</i>	392239	393642	(P)	Putative enzymes	Putative auto-transporter

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
222	382		<i>yaiV</i>	393685	394353		Hypothetical ORF, unclassified, unknown	Hypothetical outer membrane protein
223	383	EcXA051a-b	<i>rpsQ</i>	3445951	3446205	(D)	Translation, post-translational modification	
224	384		<i>rpmC</i>	3446205	3446396		Translation, post-translational modification	
225	385		<i>rplP</i>	3446396	3446806		Translation, post-translational modification	
226	386		<i>rpsC</i>	3446819	3447520		Translation, post-translational modification	
227	387		<i>rplV</i>	3447538	3447870		Translation, post-translational modification	
228	388		<i>rpsS</i>	3447885	3448163		Translation, post-translational modification	
229	389		<i>rplB</i>	3448180	3449001		Translation, post-translational modification	Translation
230	390		<i>rplW</i>	3449019	3449321		Translation, post-translational modification	Translation
231	391		<i>rplD</i>	3449318	3449923		Translation, post-translational modification	
232	392		<i>rplC</i>	3449934	3450563		Translation, post-translational modification	
233	393		<i>rpsJ</i>	3450596	3450907		Translation, post-translational modification	
234	394	EcXA052	<i>rplT</i>	1797417	1797773	(D)	Translation, post-translational modification	
235	395		<i>rplM</i>	1797826	1798023		Translation, post-translational modification	
236	396		<i>infC</i>	1798120	1798662		Translation, post-translational modification	Translation

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
237	397		<i>thrS</i>	1798666	1800594		Translation, post-translational modification	
238	398	EcXA053	<i>gor</i>	3643929	3645281	(P)	Biosynthesis of cofactors, prosthetic groups and carriers	Glutathione oxidoreductase
		EcXA054	Same operon as EcXA031					
239	399	EcXA055	<i>rrlG</i>	2724301	2727204	(D)	Translation, post-translational modification	Translation (rRNA)
240	400		<i>rrlG</i>	2724089	2724208		Translation, post-translational modification	Translation (rRNA)
241	401		<i>gltW</i>	2727389	2727464		Translation, post-translational modification	Translation (tRNA)
242	402		<i>rrsG</i>	2727636	2729178		Translation, post-translational modification	Translation (rRNA)

Several of the expression vectors contain fragments that correspond to genes of unknown function or if the function is known, it is not known whether the gene is essential. For example, EcXA001, 003, 007, 008, 013, 015, 016, 017, 018, 019, 020, 021, 022, 023, 024, 025, 026, 027, 028, 029, 030, 032, 033, 034, 035, 036, 037, 038, 039, 040, 041, 047, 048, 049 and 050 are all exogenous nucleic acid sequences that correspond to *E. coli* proteins that have no known function or where the function has not been shown to be essential or nonessential.

The present invention reports a number of novel *E. coli* genes and operons that are required for proliferation. From the list clone sequences identified here, each was identified to be a portion of a gene in an operon required for the proliferation of *E. coli*. Cloned sequences corresponding to genes already known to be required for proliferation in *E. coli* include EcXA002, 004, 005, 010, 012, 014, 031, 02, 043, 045, 051, 052, 054, and 055. The remaining identified sequences correspond to *E. coli* genes previously undesignated as required for proliferation in the art.

An interesting observation of the present invention is that there are also several sequence fragments that correspond to *E. coli* genes that are not thought to be required for *E. coli* proliferation. Nevertheless, under the conditions described above, the antisense expression of these gene fragments causes a reduction in cell growth. This result implies that the genes corresponding to the identified sequences are actually required for proliferation. Molecule Nos. corresponding to these genes are EcXA006, 044, 046, and 053.

Following identification of the sequences of interest, these sequences were localized into operons. Since bacterial genes are expressed in a polycistronic manner, the antisense inhibition of a single gene in an operon might effect the expression of all the other genes on the operon or the genes down stream from the single gene identified. In order to determine which of the gene products in an operon are required for proliferation, each of the genes contained within an operon may be analyzed for their effect on viability as described below.

TABLE III

Operon Boundaries

Mole. No.	Left Coordinate	Right Coordinate
EcXA001	3606848	3608143
EcXA002	2702355	2703329
EcXA003	1015762	1017522
EcXA004	3467782	3472189
EcXA005	4177574	4178503
EcXA006	2412767	2414911
EcXA007	3841591	3843357
EcXA008	3268266	3272548
EcXA009	1599514	1605313
EcXA010	1647406	1647458
EcXA011	1545425	1550015
EcXA012	3467782	3472189
EcXA013	2697683	2697943
EcXA014	3049135	3053470
EcXA015	2465875	2468482
EcXA016	1877031	1877972
EcXA017	3065360	3066100
EcXA018	2151891	2160901
EcXA019	2185400	2190242
EcXA020	1877031	1877972
EcXA021	238746	239084
EcXA022	1703791	1710182
EcXA023	1585817	1588025
EcXA024	3231369	3232096
EcXA025	2042885	2050036
EcXA026	331001	331184
EcXA027c	2225343	2228405
EcXA028	2420669	2421559
EcXA029	4626424	4628091
EcXA030	3718309	3719678
EcXA031	3440255	3445786
EcXA032b	751452	753691
EcXA033	3192961	3198606
EcXA034	3717678	3717890
EcXA035	3694087	3697522
EcXA036	3246594	3248594
EcXA037	1620984	1621874
EcXA038	1416572	1417368
EcXA039	522485	528354
EcXA040	3580669	3580672
EcXA041	1196090	1197460
EcXA042	2280537	2280821

Mole. No.	Left Coordinate	Right Coordinate
EcXA043	765207	773404
EcXA044	1189839	1191209
EcXA045	2816575	2817168
EcXA046	4538525	4547279
EcXA047	1637054	1639578
EcXA048	2099917	2106351
EcXA049	402927	404042
EcXA050	392239	394353
EcXA051	3445951	3450907
EcXA052	1797417	1800594
EcXA053	3643929	3645281
EcXA054	3440255	3445786
EcXA055	2724301	2729178

### EXAMPLE 5

#### Identification of Individual Genes within an Operon Required for Proliferation

The following example illustrates a method for determining which gene in an operon is required for proliferation. The clone insert corresponding to Molecule No. EcXA004 possesses nucleic acid sequence homology to the *E. coli* genes *rspG* and *rspL*. This molecule corresponds to an operon containing two additional genes *fusA* and *tufA*. The *rspL* gene is the first gene in the operon. To determine which gene or genes in this operon are required for proliferation, each gene is selectively inactivated using homologous recombination. Gene *rspL* is the first gene to be inactivated.

Deletion inactivation of a chromosomal copy of a gene in *E. coli* can be accomplished by integrative gene replacement. The principle of this method (Hamilton, C. M., et al 1989. *J. Bacteriol.* 171: 4617-4622) is to construct a mutant allele of the targeted gene, introduce that allele into the chromosome using a conditional suicide vector, and then force the removal of the native wild type allele and vector sequences. This will replace the native gene with a desired mutation(s) but leave promoters, operators, etc. intact. Essentiality of a gene is determined either by deduction from genetic analysis or by conditional expression of a wild type copy of the targeted gene (trans complementation).

The first step is to generate a mutant *rspL* allele using PCR amplification. Two sets of PCR primers are chosen to produce a copy of *rspL* with a large central deletion to inactivate the gene. In order to eliminate polar effects, it is desirable to construct a mutant allele comprising an in-frame deletion of most or all of the coding region of the *rspL* gene. Each set of PCR primers is chosen such that a region flanking the gene to be amplified is sufficiently long to allow recombination (typically at least 500 nucleotides on each side of the deletion). The targeted deletion or mutation will be contained within this fragment. To facilitate cloning of the PCR product, the PCR primers may also contain restriction endonuclease sites found in the cloning region of a conditional knockout vector such as pK03 (Link, et al 1997 *J. Bacteriol.* 179 (20): 6228-6237). Suitable sites include NotI, Sall, BamHI and SmaI. The *rspL* gene fragments are produced using standard PCR conditions including, but not limited to, those outlined in the manufacturers directions for the



Hot Start Taq PCR kit (Qiagen, Inc., Valencia, CA). The PCR reactions will produce two fragments that can be fused together. Alternatively, crossover PCR can be used to generate a desired deletion in one step (Ho, S. N., et al 1989. *Gene* 77: 51-59, Horton, R. M., et al 1989. *Gene* 77: 61-68). The mutant allele thus produced is called a "null" allele because it cannot produce a functional gene product.

5 The mutant allele obtained from PCR amplification is cloned into the multiple cloning site of pK03. Directional cloning of the *rpsL* null allele is not necessary. The pK03 vector has a temperature-sensitive origin of replication derived from pSC101. Therefore, clones are propagated at the permissive temperature of 30°C. The vector also contains two selectable marker genes: one that confers resistance to chloramphenicol and another, the *Bacillus subtilis* *sacB* gene, that allows for counter-selection on sucrose containing growth medium. Clones that contain vector DNA with the null allele  
10 inserted are confirmed by restriction endonuclease analysis and DNA sequence analysis of isolated plasmid DNA. The plasmid containing the *rpsL* null allele insert is known as a knockout plasmid.

Once the knockout plasmid has been constructed and its sequence verified, it is transformed into a Rec<sup>+</sup> *E. coli* host cell. Transformation can be by any standard method such as electroporation. In some fraction of the transformed cells, plasmids will integrate into the *E. coli* chromosome by homologous recombination between the *rpsL* null allele in the  
15 plasmid and the *rpsL* gene in the chromosome. Transformant colonies in which such an event has occurred are readily selected by growth at the non-permissive temperature of 43°C and in the presence of chloramphenicol. At this temperature, the plasmid will not replicate as an episome and will be lost from cells as they grow and divide. These cells are no longer resistant to chloramphenicol and will not grow when it is present. However, cells in which the knockout plasmid has integrated into the *E. coli* chromosome remain resistant to chloramphenicol and propagate.

20 Cells containing integrated knock-out plasmids are usually the result of a single crossover event that creates a tandem repeat of the mutant and native wild type alleles of *rpsL* separated by the vector sequences. A consequence of this is that *rpsL* will still be expressed in these cells. In order to determine if the gene is essential for growth, the wild type copy must be removed. This is accomplished by selecting for plasmid excision, a process in which homologous recombination between the two alleles results in looping out of the plasmid sequences. Cells that have undergone such an  
25 excision event and have lost plasmid sequences including *sacB* gene are selected for by addition of sucrose to the medium. The *sacB* gene product converts sucrose to a toxic molecule. Thus counter selection with sucrose ensures that plasmid sequences are no longer present in the cell. Loss of plasmid sequences is further confirmed by testing for sensitivity to chloramphenicol (loss of the chloramphenicol resistance gene). The latter test is important because occasionally a mutation in the *sacB* gene can occur resulting in a loss of *sacB* function with no effect on plasmid replication (Link, et. al.,  
30 1997 *J. Bacteriol.* 179 (20): 6228-6237). These artifact clones retain plasmid sequences and are therefore still resistant to chloramphenicol.

In the process of plasmid excision, one of the two *rpsL* alleles is lost from the chromosome along with the plasmid DNA. In general, it is equally likely that the null allele or the wild type allele will be lost. Therefore, if the *rpsL*

gene is not essential, half of the clones obtained in this experiment will have the wild type allele on the chromosome and half will have the null allele. However, if the *rpsL* gene is essential, cells containing the null allele will not be obtained as a single copy of the null allele would be lethal.

To determine the essentiality of *rpsL*, a statistically significant number of the resulting clones, at least 20, are analyzed by PCR amplification of the *rpsL* gene. Since the null allele is missing a significant portion of the *rpsL* gene, its PCR product is significantly shorter than that of the wild type gene and the two are readily distinguished by gel electrophoretic analysis. The PCR products may also be subjected to sequence determination for further confirmation by methods well known to those in the art.

The above experiment is generally adequate for determining the essentiality of a gene such as *rpsL*. However, it may be necessary or desirable to more directly confirm the essentiality of the gene. There are several methods by which this can be accomplished. In general, these involve three steps: 1) construction of an episome containing a wild type allele, 2) isolation of clones containing a single chromosomal copy of the mutant null allele as described above but in the presence of the episomal wild type allele, and then 3) determining if the cells survive when the expression of the episomal allele is shut off. In this case, the trans copy of wild type *rpsL* is made by PCR cloning of the entire coding region of *rpsL* and inserting it in the sense orientation downstream of an inducible promoter such as the *E. coli lac* promoter. Transcription of this allele of *rpsL* will be induced in the presence of IPTG which inactivates the *lac* repressor. Under IPTG induction *rpsL* protein will be expressed as long as the recombinant gene also possesses a ribosomal binding site, also known as a "Shine-Dalgarno Sequence". The trans copy of *rpsL* is cloned on a plasmid that is compatible with pSC101. Compatible vectors include p15A, pBR322, and the pUC plasmids, among others. Replication of the compatible plasmid will not be temperature-sensitive. The entire process of integrating the null allele of *rpsL* and subsequent plasmid excision is carried out in the presence of IPTG to ensure the expression of functional *rpsL* protein is maintained throughout. After the null *rpsL* allele is confirmed as integrated on the chromosome in place of the wild type *rpsL* allele, then IPTG is withdrawn and expression of functional *rpsL* protein shut off. If the *rpsL* gene is essential, cells will cease to proliferate under these conditions. However, if the *rpsL* gene is not essential, cells will continue to proliferate under these conditions. In this experiment, essentiality is determined by conditional expression of a wild type copy of the gene rather than inability to obtain the intended chromosomal disruption.

An advantage of this method over some other gene disruption techniques is that the targeted gene can be deleted or mutated without the introduction of large segments of foreign DNA. Therefore, polar effects on downstream genes are eliminated or minimized. There are methods described to introduce inducible promoters upstream of potential essential bacterial genes. However in such cases, polarity from multiple transcription start points can be a problem. One way of preventing this is to insert a gene disruption cassette that contains strong transcriptional terminators upstream of the integrated inducible promoter (Zhang, Y, and Cronan, J. E. 1996 *J. Bacteriol.* 178 (12): 3614-3620). The described techniques will all be familiar to one of ordinary skill in the art.

Following the analysis of the *rpsL* gene, the other genes of the operon are investigated to determine if they are required for proliferation.

### EXAMPLE 6

#### Expression of the Proteins Encoded by Genes Identified as Required for *E. coli* Proliferation

5 The following is provided as one exemplary method to express the proliferation-required proteins encoded by the identified sequences described above. First, the initiation and termination codons for the gene are identified. If desired, methods for improving translation or expression of the protein are well known in the art. For example, if the nucleic acid encoding the polypeptide to be expressed lacks a methionine codon to serve as the initiation site, a strong Shine-Delgarno sequence, or a stop codon, these sequences can be added. Similarly, if the identified nucleic acid sequence lacks a transcription  
10 termination signal, this sequence can be added to the construct by, for example, splicing out such a sequence from an appropriate donor sequence. In addition, the coding sequence may be operably linked to a strong promoter or an inducible promoter if desired. The identified nucleic acid sequence or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial expression vector or genome using oligonucleotide primers complementary to the identified nucleic acid sequence or portion thereof and containing restriction endonuclease sequences for *NcoI* incorporated into the 5' primer and  
15 *BglI* at the 5' end of the corresponding 3'-primer, taking care to ensure that the identified nucleic acid sequence is positioned in frame with the termination signal. The purified fragment obtained from the resulting PCR reaction is digested with *NcoI* and *BglI*, purified and ligated to an expression vector.

The ligated product is transformed into DH5 $\alpha$  or some other *E. coli* strain suitable for the over expression of potential proteins. Transformation protocols are well known in the art. For example, transformation protocols are described in: **Current  
20 Protocols in Molecular Biology**, Vol. 1, Unit 1.8, (Ausubel, et al., Eds.) John Wiley & Sons, Inc. (1997). Positive transformants are selected after growing the transformed cells on plates containing 50-100  $\mu$ g/ml Ampicillin (Sigma, St. Louis, Missouri). In one embodiment, the expressed protein is held in the cytoplasm of the host organism. In an alternate embodiment, the expressed protein is released into the culture medium. In still another alternative, the expressed protein can be sequestered in the periplasmic space and liberated therefrom using any one of a number of cell lysis techniques known in the art. For  
25 example, the osmotic shock cell lysis method described in Chapter 16 of **Current Protocols in Molecular Biology**, Vol. 2, (Ausubel, et al., Eds.) John Wiley & Sons, Inc. (1997). Each of these procedures can be used to express a proliferation-required protein.

Expressed proteins, whether in the culture medium or liberated from the periplasmic space or the cytoplasm, are then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, standard  
30 chromatography, immunoprecipitation, immunochromatography, size exclusion chromatography, ion exchange chromatography, and HPLC. Alternatively, the secreted protein can be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment. The purity of the protein product

obtained can be assessed using techniques such as Coomassie or silver staining or using antibodies against the control protein. Coomassie and silver staining techniques are familiar to those skilled in the art.

Antibodies capable of specifically recognizing the protein of interest can be generated using synthetic peptides using methods well known in the art. See, *Antibodies: A Laboratory Manual*, (Harlow and Lane, Eds.) Cold Spring Harbor Laboratory (1988). For example, 15-mer peptides having a sequence encoded by the appropriate identified gene sequence of interest or portion thereof can be chemically synthesized. The synthetic peptides are injected into mice to generate antibodies to the polypeptide encoded by the identified nucleic acid sequence of interest or portion thereof. Alternatively, samples of the protein expressed from the expression vectors discussed above can be purified and subjected to amino acid sequencing analysis to confirm the identity of the recombinantly expressed protein and subsequently used to raise antibodies. An Example describing in detail the generation of monoclonal and polyclonal antibodies appears in Example 7.

The protein encoded by the identified nucleic acid sequence of interest or portion thereof can be purified using standard immunochromatography techniques. In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques. These procedures are well known in the art.

In an alternative protein purification scheme, the identified nucleic acid sequence of interest or portion thereof can be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies the coding sequence of the identified nucleic acid sequence of interest or portion thereof is inserted in-frame with the gene encoding the other half of the chimera. The other half of the chimera can be maltose binding protein (MBP) or a nickel binding polypeptide encoding sequence. A chromatography matrix having antibody to MBP or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites can be engineered between the MBP gene or the nickel binding polypeptide and the identified expected gene of interest, or portion thereof. Thus, the two polypeptides of the chimera can be separated from one another by protease digestion.

One useful expression vector for generating maltose binding protein fusion proteins is pMAL (New England Biolabs), which encodes the *malE* gene. In the pMal protein fusion system, the cloned gene is inserted into a pMal vector downstream from the *malE* gene. This results in the expression of an MBP-fusion protein. The fusion protein is purified by affinity chromatography. These techniques as described are well known to those skilled in the art of molecular biology.

#### EXAMPLE 7

##### Production of an Antibody to an isolated *E. coli* Protein

Substantially pure protein or polypeptide is isolated from the transformed cells as described in Example 6. The concentration of protein in the final preparation is adjusted, for example, by concentration on a 10,000 molecular weight cut off

AMICON filter device (Millipore, Bedford, MA), to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

#### Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., *Nature* 256:495 (1975) or any of the well-known derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as described by Engvall, E., "Enzyme immunoassay ELISA and EMIT," *Meth. Enzymol.* 70:419 (1980), and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. *Basic Methods in Molecular Biology* Elsevier, New York. Section 21-2.

#### Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogeneous epitopes of a single protein or a peptide can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than larger molecules and can require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. *J. Clin. Endocrinol. Metab.* 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: *Handbook of Experimental Immunology* D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 M). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: *Manual of Clinical Immunology*, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980).

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to

identify the presence of antigen in a biological sample. The antibodies can also be used in therapeutic compositions for killing bacterial cells expressing the protein.

## EXAMPLE 8

### Screening Chemical Libraries

#### A. Protein-Based Assays

Having isolated and expressed bacterial proteins shown to be required for bacterial proliferation, the present invention further contemplates the use of these expressed proteins in assays to screen libraries of compounds for potential drug candidates. The generation of chemical libraries is well known in the art. For example combinatorial chemistry can be used to generate a library of compounds to be screened in the assays described herein. A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis by combining a number of chemical "building blocks" reagents. For example, a linear combinatorial chemical library such as a polypeptide library is formed by combining amino acids in every possible combination to yield peptides of a given length. Millions of chemical compounds theoretically can be synthesized through such combinatorial mixings of chemical building blocks. For example, one commentator observed that the systematic, combinatorial mixing of 100 interchangeable chemical building blocks results in the theoretical synthesis of 100 million tetrameric compounds or 10 billion pentameric compounds. (Gallop et al., "Applications of Combinatorial Technologies to Drug Discovery, Background and Peptide Combinatorial Libraries," *Journal of Medicinal Chemistry*, Vol. 37, No. 9, 1233-1250 (1994). Other chemical libraries known to those in the art may also be used, including natural product libraries.

Once generated, combinatorial libraries can be screened for compounds that possess desirable biological properties. For example, compounds which may be useful as drugs or to develop drugs would likely have the ability to bind to the target protein identified, expressed and purified as discussed above. Further, if the identified target protein is an enzyme, candidate compounds would likely interfere with the enzymatic properties of the target protein. Any enzyme can be a target protein. For example, the enzymatic function of a target protein can be to serve as a protease, nuclease, phosphatase, dehydrogenase, transporter protein, transcriptional enzyme, and any other type of enzyme known or unknown. Thus, the present invention contemplates using the protein products described above to screen combinatorial chemical libraries.

Those in the art will appreciate that a number of techniques exist for characterizing target proteins in order to identify molecules useful for the discovery and development of therapeutics. For example, some techniques involve the generation and use of small peptides to probe and analyze target proteins both biochemically and genetically in order to identify and develop drug leads. Such techniques include the methods described in PCT publications No. W09935494, W09819162, W09954728, the disclosures of which are incorporated herein by reference in their entireties.

In another example, the target protein is a serine protease and the substrate of the enzyme is known. The present example is directed towards the analysis of libraries of compounds to identify compounds that function as inhibitors of the target enzyme. First, a library of small molecules is generated using methods of combinatorial library formation well known in

the art. U.S. Patent NOs. 5,463,564 and 5,574, 656, to Agrafiotis, et al., entitled "System and Method of Automatically Generating Chemical Compound with Desired Properties," are two such teachings. Then the library compounds are screened to identify library compounds that possess desired structural and functional properties. U.S. Patent No. 5,684,711 also discusses a method for screening libraries.

5 To illustrate the screening process, the combined target and chemical compounds of the library are exposed to and permitted to interact with the purified enzyme. A labeled substrate is added to the incubation. The label on the substrate is such that a detectable signal is emitted from metabolized substrate molecules. The emission of this signal permits one to measure the effect of the combinatorial library compounds on the enzymatic activity of target enzymes. The characteristics of each library compound is encoded so that compounds demonstrating activity against the enzyme can be analyzed and features  
10 common to the various compounds identified can be isolated and combined into future iterations of libraries.

Once a library of compounds is screened, subsequent libraries are generated using those chemical building blocks that possess the features shown in the first round of screen to have activity against the target enzyme. Using this method, subsequent iterations of candidate compounds will possess more and more of those structural and functional features required to inhibit the function of the target enzyme, until a group of enzyme inhibitors with high specificity for the enzyme can be found.  
15 These compounds can then be further tested for their safety and efficacy as antibiotics for use in mammals.

It will be readily appreciated that this particular screening methodology is exemplary only. Other methods are well known to those skilled in the art. For example, a wide variety of screening techniques are known for a large number of naturally-occurring targets when the biochemical function of the target protein is known.

#### B. Cell Based Assays

20 Current cell-based assays used to identify or to characterize compounds for drug discovery and development frequently depend on detecting the ability of a test compound to inhibit the activity of a target molecule located within a cell or located on the surface of a cell. Most often such target molecules are proteins such as enzymes, receptors and the like. However, target molecules may also include other molecules such as DNAs, lipids, carbohydrates and RNAs including messenger RNAs, ribosomal RNAs, tRNAs and the like. A number of highly sensitive cell-based assay methods are  
25 available to those of skill in the art to detect binding and interaction of test compounds with specific target molecules. However, these methods are generally not highly effective when the test compound binds to or otherwise interacts with its target molecule with moderate or low affinity. In addition, the target molecule may not be readily accessible to a test compound in solution, such as when the target molecule is located inside the cell or within a cellular compartment such as the periplasm of a bacterial cell. Thus, current cell-based assay methods are limited in that they are not effective in  
30 identifying or characterizing compounds that interact with their targets with moderate to low affinity or compounds that interact with targets that are not readily accessible.

Cell-based assay methods of the present invention have substantial advantages over current cell-based assays practiced in the art. These advantages derive from the use of sensitized cells in which the level or activity of a

proliferation-required gene product (the target molecule) has been specifically reduced to the point where the presence or absence of its function becomes a rate-determining step for cellular proliferation. Bacterial, fungal, plant, or animal cells can all be used with the present method. Such sensitized cells become much more sensitive to compounds that are active against the affected target molecule. Thus, cell-based assays of the present invention are capable of detecting compounds exhibiting low or moderate potency against the target molecule of interest because such compounds are substantially more potent on sensitized cells than on non-sensitized cells. The affect may be such that a test compound may be two to several times more potent, at least 10 times more potent or even at least 100 times more potent when tested on the sensitized cells as compared to the non-sensitized cells.

Due in part to the increased appearance of antibiotic resistance in pathogenic microorganisms and to the significant side-effects associated with some currently used antibiotics, novel antibiotics acting at new targets are highly sought after in the art. Yet, another limitation in the current art related to cell-based assays is the problem of identifying hits against the same kinds of target molecules in the same limited set of biological pathways over and over again. This may occur when compounds acting at such new targets are discarded, ignored or fail to be detected because compounds acting at the "old" targets are encountered more frequently and are more potent than compounds acting at the new targets. As a result, the majority of antibiotics in use currently interact with a relatively small number of target molecules within an even more limited set of biological pathways.

The use of sensitized cells of the current invention provides a solution to the above problem in two ways. First, desired compounds acting at a target of interest, whether a new target or a previously known but poorly exploited target, can now be detected above the "noise" of compounds acting at the "old" targets due to the specific and substantial increase in potency of such desired compounds when tested on the sensitized cells of the current invention. Second, the methods used to sensitize cells to compounds acting at a target of interest may also sensitize these cells to compounds acting at other target molecules within the same biological pathway. For example, expression of an antisense molecule to a gene encoding a ribosomal protein is expected to sensitize the cell to compounds acting at that ribosomal protein and may also sensitize the cells to compounds acting at any of the ribosomal components (proteins or rRNA) or even to compounds acting at any target which is part of the protein synthesis pathway. Thus an important advantage of the present invention is the ability to reveal new targets and pathways that were previously not readily accessible to drug discovery methods.

Sensitized cells of the present invention are prepared by reducing the activity or level of a target molecule. The target molecule may be a gene product, such as an RNA or polypeptide produced from the proliferation-required nucleic acids described herein. Alternatively, the target may be a gene product such as an RNA or polypeptide which is produced form a sequence within the same operon as the proliferation-required nucleic acids described herein. In addition, the target may be an RNA or polypeptide in the same biological pathway as the proliferation-required nucleic acids described herein.



Such biological pathways include, but are not limited to, enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such the cell wall.

Current methods employed in the arts of medicinal and combinatorial chemistries are able to make use of structure-activity relationship information derived from testing compounds in various biological assays including direct binding assays and cell-based assays. Occasionally compounds are directly identified in such assays that are sufficiently potent to be developed as drugs. More often, initial hit compounds exhibit moderate or low potency. Once a hit compound is identified with low or moderate potency, directed libraries of compounds are synthesized and tested in order to identify more potent leads. Generally these directed libraries are combinatorial chemical libraries consisting of compounds with structures related to the hit compound but containing systematic variations including additions, subtractions and substitutions of various structural features. When tested for activity against the target molecule, structural features are identified that either alone or in combination with other features enhance or reduce activity. This information is used to design subsequent directed libraries containing compounds with enhanced activity against the target molecule. After one or several iterations of this process, compounds with substantially increased activity against the target molecule are identified and may be further developed as drugs. This process is facilitated by use of the sensitized cells of the present invention since compounds acting at the selected targets exhibit increased potency in such cell-based assays, thus; more compounds can now be characterized providing more useful information than would be obtained otherwise.

Thus, it is now possible using cell-based assays of the present invention to identify or characterize compounds that previously would not have been readily identified or characterized including compounds that act at targets that previously were not readily exploited using cell-based assays. The process of evolving potent drug leads from initial hit compounds is also substantially improved by the cell-based assays of the present invention because, for the same number of test compounds, more structure-function relationship information is likely to be revealed.

The method of sensitizing a cell entails selecting a suitable gene or operon. A suitable gene or operon is one whose expression is required for the proliferation of the cell to be sensitized. The next step is to introduce into the cells to be sensitized, an antisense RNA capable of hybridizing to the suitable gene or operon or to the RNA encoded by the suitable gene or operon. Introduction of the antisense RNA can be in the form of an expression vector in which antisense RNA is produced under the control of an inducible promoter. The amount of antisense RNA produced is limited by varying the inducer concentration to which the cell is exposed and thereby varying the activity of the promoter driving transcription of the antisense RNA. Thus, cells are sensitized by exposing them to an inducer concentration that results in a sub-lethal level of antisense RNA expression.

In one embodiment of the cell-based assays, the identified exogenous *E. coli* nucleotide sequences of the present invention are used to inhibit the production of a proliferation-required protein. Expression vectors producing antisense RNA against identified genes required for proliferation are used to limit the concentration of a proliferation-required protein without severely inhibiting growth. To achieve that goal, a growth inhibition dose curve of inducer is calculated by plotting

various doses of inducer against the corresponding growth inhibition caused by the antisense expression. From this curve, various percentages of antisense induced growth inhibition, from 1 to 100% can be determined. If the promoter contained in the expression vector contains a */ac* operator the transcription is regulated by */ac* repressor and expression from the promoter is inducible with IPTG. For example, the highest concentration of the inducer IPTG that does not reduce the growth rate (0% growth inhibition) can be predicted from the curve. Cellular proliferation can be monitored by growth medium turbidity via OD measurements. In another example, the concentration of inducer that reduces growth by 25% can be predicted from the curve. In still another example, a concentration of inducer that reduces growth by 50% can be calculated. Additional parameters such as colony forming units (cfu) can be used to measure cellular viability.

Cells to be assayed are exposed to the above-determined concentrations of inducer. The presence of the inducer at this sub-lethal concentration reduces the amount of the proliferation required gene product to the lowest amount in the cell that will support growth. Cells grown in the presence of this concentration of inducer are therefore specifically more sensitive to inhibitors of the proliferation-required protein or RNA of interest or to inhibitors of proteins or RNAs in the same biological pathway as the proliferation-required protein or RNA of interest but not to inhibitors of unrelated proteins or RNAs.

Cells pretreated with sub-inhibitory concentrations of inducer and thus containing a reduced amount of proliferation-required target gene product are then used to screen for compounds that reduce cell growth. The sub-lethal concentration of inducer may be any concentration consistent with the intended use of the assay to identify candidate compounds to which the cells are more sensitive. For example, the sub-lethal concentration of the inducer may be such that growth inhibition is at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60% at least about 75%, or more. Cells which are pre-sensitized using the preceding method are more sensitive to inhibitors of the target protein because these cells contain less target protein to inhibit than wild-type cells.

In another embodiment of the cell based assays of the present invention, the level or activity of a proliferation required gene product is reduced using a temperature sensitive ...mutation in the proliferation-required sequence and an antisense nucleic acid against the proliferation-required sequence. Growing the cells at an intermediate temperature between the permissive and restrictive temperatures of the temperature sensitive mutant where the mutation is in a proliferation-required gene produces cells with reduced activity of the proliferation-required gene product. The antisense RNA directed against the proliferation-required sequence further reduces the activity of the proliferation required gene product. Drugs that may not have been found using either the temperature sensitive mutation or the antisense nucleic acid alone may be identified by determining whether cells in which expression of the antisense nucleic acid has been induced and which are grown at a temperature between the permissive temperature and the restrictive temperature are substantially more sensitive to a test compound than cells in which expression of the antisense nucleic acid has not been induced and which are grown at a permissive temperature. Also drugs found previously from either the antisense nucleic acid alone or the

temperature sensitive mutation alone may have a different sensitivity profile when used in cells combining the two approaches, and that sensitivity profile may indicate a more specific action of the drug in inhibiting one or more activities of the gene product.

5 Temperature sensitive mutations may be located at different sites within the gene and correspond to different domains of the protein. For example, the *dnaB* gene of *Escherichia coli* encodes the replication fork DNA helicase. DnaB has several domains, including domains for oligomerization, ATP hydrolysis, DNA binding, interaction with primase, interaction with DnaC, and interaction with DnaA [(Biswas, E.E. and Biswas, S.B. 1999. Mechanism and DnaB helicase of *Escherichia coli*: structural domains involved in ATP hydrolysis, DNA binding, and oligomerization. *Biochem.* 38:10919-10928; Hiasa, H. and Marians, K.J. 1999. Initiation of bidirectional replication at the chromosomal origin is directed by the interaction between helicase and primase. *J. Biol. Chem.* 274:27244-27248; San Martin, C., Radermacher, M., Wolpensinger, B., Engel, A., Miles, C.S., Dixon, N.E., and Carazo, J.M. 1998. Three-dimensional reconstructions from cryoelectron microscopy images reveal an intimate complex between helicase DnaB and its loading partner DnaC. *Structure* 6:501-9; Sutton, M.D., Carr, K.M., Vicente, M., and Kaguni, J.M. 1998. *Escherichia coli* DnaA protein. The N-terminal domain and loading of DnaB helicase at the *E. coli* chromosomal. *J. Biol. Chem.* 273:34255-62.), the disclosures of which are incorporated herein by reference in their entireties]. Temperature sensitive mutations in different domains of DnaB confer different phenotypes at the restrictive temperature, which include either an abrupt stop or slow stop in DNA replication with or without DNA breakdown (Wechsler, J.A. and Gross, J.D. 1971. *Escherichia coli* mutants temperature-sensitive for DNA synthesis. *Mol. Gen. Genetics* 113:273-284, the disclosure of which is incorporated herein by reference in its entirety) and termination of growth or cell death. Combining the use of temperature sensitive mutations in the *dnaB* gene that cause cell death at the restrictive temperature with an antisense to the *dnaB* gene could lead to the discovery of very specific and effective inhibitors of one or a subset of activities exhibited by DnaB.

20 When screening for antimicrobial agents against a gene product required for proliferation, growth inhibition of cells containing a limiting amount of that proliferation-required gene product can be assayed. Growth inhibition can be measured by directly comparing the amount of growth, measured by the optical density of the growth medium, between an experimental sample and a control sample. Alternative methods for assaying cell proliferation include measuring green fluorescent protein (GFP) reporter construct emissions, various enzymatic activity assays, and other methods well known in the art.

25 It will be appreciated that the above method may be performed in solid phase, liquid phase or a combination of the two. For example, cells grown on nutrient agar containing the inducer of the antisense construct may be exposed to compounds spotted onto the agar surface. A compound's effect may be judged from the diameter of the resulting killing zone, the area around the compound application point in which cells do not grow. Multiple compounds may be transferred to agar plates and simultaneously tested using automated and semi-automated equipment including but not restricted to

multi-channel pipettes (for example the Beckman Multimek) and multi-channel spotters (for example the Genomic Solutions Flexys). In this way multiple plates and thousands to millions of compounds may be tested per day.

The compounds may also be tested entirely in liquid phase using microtiter plates as described below. Liquid phase screening may be performed in microtiter plates containing 96, 384, 1536 or more wells per microtiter plate to screen multiple plates and thousands to millions of compounds per day. Automated and semi-automated equipment may be used for addition of reagents (for example cells and compounds) and determination of cell density.

#### EXAMPLE 9

The effectiveness of the above cell based assay was validated using constructs expressing antisense RNA to *E. coli* genes *rplL*, *rplJ*, and *rplW* encoding ribosomal proteins L7/L12, L10 and L23 respectively. These proteins are part of the protein synthesis apparatus of the cell and as such are required for proliferation. These constructs were used to test the effect of antisense expression on cell sensitivity to antibiotics known to bind to the ribosome and thereby inhibit protein synthesis. Constructs expressing antisense RNA to several other genes (*elaD*, *visC*, *yohH*, and *aptE/B*), the products of which are not involved in protein synthesis were used for comparison.

First expression vectors containing antisense constructs to either *rplW* or to *elaD* were introduced into separate *E. coli* cell populations. Vector introduction is a technique well known to those of ordinary skill in the art. The expression vectors of this example contain IPTG inducible promoters that drive the expression of the antisense RNA in the presence of the inducer. However, those skilled in the art will appreciate that other inducible promoters may also be used. Suitable expression vectors are also well known in the art. The *E. coli* antisense clones encoding ribosomal proteins L7/L12, L10 and L23 were used to test the effect of antisense expression on cell sensitivity to the antibiotics known to bind to these proteins. First, expression vectors containing antisense to either the genes encoding L7/L12 and L10 or L23 were introduced into separate *E. coli* cell populations.

The cell populations were exposed to a range of IPTG concentrations in liquid medium to obtain the growth inhibitory dose curve for each clone (Fig. 1). First, seed cultures were grown to a particular turbidity that is measured by the optical density (OD) of the growth solution. The OD of the solution is directly related to the number of bacterial cells contained therein. Subsequently, sixteen 200  $\mu$ l liquid medium cultures were grown in a 96 well microtiter plate at 37 C with a range of IPTG concentrations in duplicate two-fold serial dilutions from 1600  $\mu$ M to 12.5  $\mu$ M (final concentration). Additionally, control cells were grown in duplicate without IPTG. These cultures were started from equal amounts of cells derived from the same initial seed culture of a clone of interest. The cells were grown for up to 15 hours and the extent of growth was determined by measuring the optical density of the cultures at 600 nm. When the control culture reached mid-log phase the percent growth of the control for each of the IPTG containing cultures was plotted against the log concentrations of IPTG to produce a growth inhibitory dose response curve for the IPTG. The concentration of IPTG that inhibits cell growth to 50% ( $IC_{50}$ ) as compared to the 0 mM IPTG control (0% growth inhibition) was then calculated from

the curve. Under these conditions, an amount of antisense RNA was produced that reduced the expression levels of *rplW* and *elaD* to a degree such that growth was inhibited by 50%.

Alternative methods of measuring growth are also contemplated. Examples of these methods include measurements of proteins, the expression of which is engineered into the cells being tested and can readily be measured. Examples of such proteins include green fluorescent protein (GFP) and various enzymes.

Cells were pretreated with the selected concentration of IPTG and then used to test the sensitivity of cell populations to tetracycline, erythromycin and other protein synthesis inhibitors. An example of a tetracycline dose response curve is shown in Figures 2A and 2B for the *rplW* and *elaD* genes, respectively. Cells were grown to log phase and then diluted into media alone or media containing IPTG at concentrations which give 20% and 50% growth inhibition as determined by IPTG dose response curves. After 2.5 hours, the cells were diluted to a final OD600 of 0.002 into 96 well plates containing (1) +/- IPTG at the same concentrations used for the 2.5 hour pre-incubation; and (2) serial two-fold dilutions of tetracycline such that the final concentrations of tetracycline range from 1 µg/ml to 15.6 ng/ml and 0 µg/ml. The 96 well plates were incubated at 37°C and the OD600 was read by a plate reader every 5 minutes for up to 15 hours. For each IPTG concentration and the no IPTG control, tetracycline dose response curves were determined when the control (absence of tetracycline) reached 0.1 OD600. To compare tetracycline sensitivity with and without IPTG, tetracycline IC50s were determined from the dose response curves (Figs. 2A-B). Cells with reduced levels of L23 (*rplW*) showed increased sensitivity to tetracycline (Fig. 2A) as compared to cells with reduced levels of *elaD* (Fig. 2B). Figure 3 shows a summary bar chart in which the ratios of tetracycline IC50s determined in the presence of IPTG which gives 50% growth inhibition versus tetracycline IC50s determined without IPTG (fold increase in tetracycline sensitivity) were plotted. Cells with reduced levels of either L7/L12 (genes *rplL*, *rplJ*) or L23 (*rplW*) showed increased sensitivity to tetracycline (Fig. 3). Cells expressing antisense to genes not known to be involved in protein synthesis (*atpB/E*, *visC*, *elaD*, *yohH*) did not show the same increased sensitivity to tetracycline, validating the specificity of this assay (Fig. 3).

In addition to the above, it has been observed in initial experiments that clones expressing antisense RNA to genes involved in protein synthesis (including genes encoding ribosomal proteins L7/L12 & L10, L7/L12 alone, L22, and L18, as well as genes encoding rRNA and Elongation Factor G) have increased sensitivity to the macrolide, erythromycin, whereas clones expressing antisense to the non-protein synthesis genes *elaD*, *atpB/E* and *visC* do not. Furthermore, the clone expressing antisense to *rplL* and *rplJ* does not show increased sensitivity to nalidixic acid and ofloxacin, antibiotics which do not inhibit protein synthesis.

The results with the ribosomal protein genes *rplL*, *rplJ*, and *rplW* as well as the initial results using various other antisense clones and antibiotics show that limiting the concentration of an antibiotic target makes cells more sensitive to the antimicrobial agents that specifically interact with that protein. The results also show that these cells are sensitized to antimicrobial agents that inhibit the overall function in which the protein target is involved but are not sensitized to antimicrobial agents that inhibit other functions.

The cell based assay described above may also be used to identify the biological pathway in which a proliferation-required nucleic acid or its gene product lies. In such methods, cells expressing a sub-lethal level of antisense to a target proliferation-required nucleic acid and control cells in which expression of the antisense has not been induced are contacted with a panel of antibiotics known to act in various pathways. If the antibiotic acts in the pathway in which the target proliferation-required nucleic acid or its gene product lies, cells in which expression of the antisense has been induced will be more sensitive to the antibiotic than cells in which expression of the antisense has not been induced.

As a control, the results of the assay may be confirmed by contacting a panel of cells expressing antisense nucleic acids to many different proliferation-required genes including the target proliferation-required gene. If the antibiotic is acting specifically, heightened sensitivity to the antibiotic will be observed only in the cells expressing antisense to a target proliferation-required gene (or cells expressing antisense to other proliferation-required genes in the same pathway as the target proliferation-required gene) but will not be observed generally in all cells expressing antisense to proliferation-required genes.

Similarly, the above method may be used to determine the pathway on which a test antibiotic acts. A panel of cells, each of which expresses antisense to a proliferation-required nucleic acid in a known pathway, is contacted with a compound for which it is desired to determine the pathway on which it acts. The sensitivity of the panel of cells to the test compound is determined in cells in which expression of the antisense has been induced and in control cells in which expression of the antisense has not been induced. If the test antibiotic acts on the pathway on which an antisense nucleic acid acts, cells in which expression of the antisense has been induced will be more sensitive to the antibiotic than cells in which expression of the antisense has not been induced. In addition, control cells in which expression of antisense to proliferation-required genes in other pathways has been induced will not exhibit heightened sensitivity to the antibiotic. In this way, the pathway on which the test antibiotic acts may be determined.

The Example below provides one method for performing such assays.

#### EXAMPLE 10

##### Identification of the Pathway in which a Proliferation-Required

##### Gene Lies or the Pathway on which an Antibiotic Acts

##### A. Preparation of Bacterial Stocks for Assay

To provide a consistent source of cells to screen, frozen stocks of host bacteria containing the desired antisense construct are prepared using standard microbiological techniques. For example, a single clone of the organism can be isolated by streaking out a sample of the original stock onto an agar plate containing nutrients for cell growth and an antibiotic for which the antisense construct contains a gene which confers resistance. After overnight growth an isolated colony is picked from the plate with a sterile needle and transferred to an appropriate liquid growth media containing the antibiotic required for maintenance of the plasmid. The cells are incubated at 30°C to 37°C with vigorous shaking for 4 to

6 hours to yield a culture in exponential growth. Sterile glycerol is added to 15% (volume to volume) and 100 $\mu$ L to 500  $\mu$ L aliquots are distributed into sterile cryotubes, snap frozen in liquid nitrogen, and stored at -80°C for future assays.

#### B. Growth of Bacteria for Use in the Assay

5 A day prior to an assay, a stock vial is removed from the freezer, rapidly thawed (37°C water bath) and a loop of culture is streaked out on an agar plate containing nutrients for cell growth and an antibiotic to which the antisense construct confers resistance. After overnight growth at 37°C, ten randomly chosen, isolated colonies are transferred from the plate (sterile inoculum loop) to a sterile tube containing 5 mL of LB medium containing the antibiotic to which the antisense vector confers resistance. After vigorous mixing to form a homogeneous cell suspension, the optical density of the suspension is measured at 600 nm (OD600) and if necessary an aliquot of the suspension is diluted into a second tube  
10 of 5 mL, sterile, LB medium plus antibiotic to achieve an  $OD_{600} \leq 0.02$  absorbance units. The culture is then incubated at 37° C for 1-2 hrs with shaking until the OD600 reaches OD 0.2 – 0.3. At this point the cells are ready to be used in the assay.

#### C. Selection of Media to be Used in Assay

15 Two fold dilution series of the inducer are generated in culture media containing the appropriate antibiotic for maintenance of the antisense construct. Several media are tested side by side and three to four wells are used to evaluate the effects of the inducer at each concentration in each media. For example, M9 minimal media, LB broth, TBD broth and Muller-Hinton media may be tested with the inducer IPTG at the following concentrations, 50  $\mu$ M, 100  $\mu$ M, 200  $\mu$ M, 400  $\mu$ M, 600  $\mu$ M, 800  $\mu$ M and 1000  $\mu$ M. Equal volumes of test media-inducer and cells are added to the wells of a 384 well microtiter plate and mixed. The cells are prepared as described above and diluted 1:100 in the appropriate media  
20 containing the test antibiotic immediately prior to addition to the microtiter plate wells. For a control, cells are also added to several wells of each media that do not contain inducer, for example 0 M IPTG. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of inducer is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without inducer. The medium yielding greatest sensitivity to inducer is  
25 selected for use in the assays described below.

#### D. Measurement of Test Antibiotic Sensitivity in the Absence of Antisense Construct Induction

30 Two-fold dilution series of antibiotics of known mechanism of action are generated in the culture media selected for further assay development that has been supplemented with the antibiotic used to maintain the construct. A panel of test antibiotics known to act on different pathways is tested side by side with three to four wells being used to evaluate the effect of a test antibiotic on cell growth at each concentration. Equal volumes of test antibiotic and cells are added to the wells of a 384 well microtiter plate and mixed. Cells are prepared as described above using the media selected for assay development supplemented with the antibiotic required to maintain the antisense construct and are diluted 1:100 in identical media immediately prior to addition to the microtiter plate wells. For a control, cells are also added to several

wells that contain the solvent used to dissolve the antibiotics but no antibiotic. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of antibiotic is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without antibiotic. A plot of percent inhibition against log[antibiotic concentration] allows extrapolation of an  $IC_{50}$  value for each antibiotic.

#### E. Measurement of Test Antibiotic Sensitivity in the Presence of Antisense Construct Inducer

The culture media selected for use in the assay is supplemented with inducer at concentrations shown to inhibit cell growth by 50 and 80% as described above and the antibiotic used to maintain the construct. Two fold dilution series of the panel of test antibiotics used above are generated in each of these media. Several antibiotics are tested side by side with three to four wells being used to evaluate the effects of an antibiotic on cell growth at each concentration, in each media. Equal volumes of test antibiotic and cells are added to the wells of a 384 well microtiter plate and mixed. Cells are prepared as described above using the media selected for use in the assay supplemented with the antibiotic required to maintain the antisense construct. The cells are diluted 1:100 into two 50 mL aliquots of identical media containing concentrations of inducer that have been shown to inhibit cell growth by 50% and 80 % respectively and incubated at 37°C with shaking for 2.5 hours. Immediately prior to addition to the microtiter plate wells, the cultures are adjusted to an appropriate  $OD_{600}$  (typically 0.002) by dilution into warm (37°C) sterile media supplemented with identical concentrations of the inducer and antibiotic used to maintain the antisense construct. For a control, cells are also added to several wells that contain solvent used to dissolve test antibiotics but which contain no antibiotic. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of antibiotic is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without antibiotic. A plot of percent inhibition against log[antibiotic concentration] allows extrapolation of an  $IC_{50}$  value for each antibiotic.

#### F. Determining the Specificity of the Test Antibiotics

A comparison of the  $IC_{50}$ s generated by antibiotics of known mechanism of action under antisense induced and non-induced conditions allows the pathway in which a proliferation-required nucleic acid lies to be identified. If cells expressing an antisense nucleic acid against a proliferation-required gene are selectively sensitive to an antibiotic acting via a particular pathway, then the gene against which the antisense acts is involved in the pathway in which the antibiotic acts.

#### G. Identification of Pathway in which a Test Antibiotic Acts

As discussed above, the cell based assay may also be used to determine the pathway against which a test antibiotic acts. In such an analysis, the pathways against which each member of a panel of antisense nucleic acids acts are identified as described above. A panel of cells, each containing an inducible antisense vector against a gene in a known proliferation-required pathway, is contacted with a test antibiotic for which it is desired to determine the pathway



on which it acts under inducing an non-inducing conditions. If heightened sensitivity is observed in induced cells expressing antisense against a gene in a particular pathway but not in induced cells expressing antisense against genes in other pathways, then the test antibiotic acts against the pathway for which heightened sensitivity was observed.

One skilled in the art will appreciate that further optimization of the assay conditions, such as the concentration of inducer used to induce antisense expression and/or the growth conditions used for the assay (for example incubation temperature and media components) may further increase the selectivity and/or magnitude of the antibiotic sensitization exhibited.

The following example confirms the effectiveness of the methods described above.

#### EXAMPLE 11

##### Identification of the Pathway in which a Proliferation-Required Gene Lies

Antibiotics of various chemical classes and modes of action were purchased from Sigma Chemicals (St. Louis, MO). Stock solutions were prepared by dissolving each antibiotic in an appropriate aqueous solution based on information provided by the manufacturer. The final working solution of each antibiotic contained no more than 0.2% (w/v) of any organic solvent. To determine their potency against a bacterial strain engineered for expression of an antisense against a proliferation-required 50S ribosomal protein, each antibiotic was serially diluted two or three fold in growth medium supplemented with the appropriate antibiotic for maintenance of the anti-sense construct. At least ten dilutions were prepared for each antibiotic. 25  $\mu$ L aliquots of each dilution were transferred to discrete wells of a 384-well microplate (the assay plate) using a multi-channel pipette. Quadruplicate wells were used for each dilution of an antibiotic under each treatment condition (plus and minus inducer). Each assay plate contained twenty wells for cell growth controls (growth media replacing antibiotic), ten wells for each treatment (plus and minus inducer, in this example IPTG). Assay plates were usually divided into the two treatments: half the plate containing induced cells and an appropriate concentrations of inducer (in this example IPTG) to maintain the state of induction, the other half containing non-induced cells in the absence of IPTG.

Cells for the assay were prepared as follows. Bacterial cells containing a construct, from which expression of antisense nucleic acid against rplL and rplJ, which encode proliferation-required 50S ribosomal subunit proteins, is inducible in the presence of IPTG, were grown into exponential growth ( $OD_{600}$  0.2 to 0.3) and then diluted 1:100 into fresh media containing either 400  $\mu$ M or 0  $\mu$ M inducer (IPTG). These cultures were incubated at 37° C for 2.5 hr. After a 2.5 hr incubation, induced and non-induced cells were respectively diluted into an assay medium at a final  $OD_{600}$  value of 0.0004. The medium contained an appropriate concentration of the antibiotic for the maintenance of the anti-sense construct. In addition, the medium used to dilute induced cells was supplemented with 800  $\mu$ M IPTG so that addition to the assay plate would result in a final IPTG concentration of 400  $\mu$ M. Induced and non-induced cell suspensions were dispensed (25  $\mu$ L/well) into the appropriate wells of the assay plate as discussed previously. The plate was then loaded into a plate reader, incubated at constant temperature, and cell growth was monitored in each well by the measurement of

light scattering at 595 nm. Growth was monitored every 5 minutes until the cell culture attained a stationary growth phase. For each concentration of antibiotic, a percentage inhibition of growth was calculated at the time point corresponding to mid-exponential growth for the associated control wells (no antibiotic, plus or minus IPTG). For each antibiotic and condition (plus or minus IPTG), a plot of percent inhibition versus log of antibiotic concentration was generated and the  $IC_{50}$  determined. A comparison of the  $IC_{50}$  for each antibiotic in the presence and absence of IPTG revealed whether induction of the antisense construct sensitized the cell to the mechanism of action exhibited by the antibiotic. Cells which exhibited a significant (standard statistical analysis) numerical decrease in the  $IC_{50}$  value in the presence of inducer were considered to have an increased sensitivity to the test antibiotic.

The results are provided in the table below, which lists the classes and names of the antibiotics used in the analysis, the targets of the antibiotics, the  $IC_{50}$  in the absence of IPTG, the  $IC_{50}$  in the presence of IPTG, the concentration units for the  $IC_{50}$ s, the fold increase in  $IC_{50}$  in the presence of IPTG, and whether increased sensitivity was observed in the presence of IPTG.

**TABLE IV**  
**Effect of Expression of Antisense RNA to rplJ and rplL on Antibiotic Sensitivity**

ANTIBIOTIC CLASS/Names	TARGET	IC50 (-IPTG)	IC50 (+IPTG)	Conc. Unit	Fold Increase in Sensitivity	Sensitivity Increased?
<b>PROTEIN SYNTHESIS INHIBITOR ANTIBIOTICS</b>						
<b>AMINOGLYCOSIDES</b>						
Gentamicin	30S ribosome function	2715	19.19	ng/ml	141	Yes
Streptomycin	30S ribosome function	11280	161	ng/ml	70	Yes
Spectinomycin	30S ribosome function	18050	< 156	ng/ml		Yes
Tobramycin	30S ribosome function	3594	70.58	ng/ml	51	Yes
<b>MACROLIDES</b>						
Erythromycin	50S ribosome function	7467	187	ng/ml	40	Yes
<b>AROMATIC POLYKETIDES</b>						
Tetracycline	30S ribosome function	199.7	1.83	ng/ml	109	Yes
Minocycline	30S ribosome function	668.4	3.897	ng/ml	172	Yes
Doxycycline	30S ribosome function	413.1	27.81	ng/ml	15	Yes
<b>OTHER PROTEIN SYNTHESIS INHIBITORS</b>						
Fusidic acid	Elongation Factor G function	59990	641	ng/ml	94	Yes
Chloramphenicol	30S ribosome function	465.4	1.516	ng/ml	307	Yes
Lincomycin	50S ribosome function	47150	324.2	ng/ml	145	Yes
<b>OTHER ANTIBIOTIC MECHANISMS</b>						
<b>B-LACTAMS</b>						
Cefoxitin	Cell wall biosynthesis	2782	2484	ng/ml	1	No
Cefotaxime	Cell wall biosynthesis	24.3	24.16	ng/ml	1	No
<b>DNA SYNTHESIS INHIBITORS</b>						
Nalidixic acid	DNA Gyrase activity	6973	6025	ng/ml	1	No
Ofloxacin	DNA Gyrase activity	49.61	45.89	ng/ml	1	No
<b>OTHER</b>						
Bacitracin	Cell membrane function	4077	4677	mg/ml	1	No
Trimethoprim	Dihydrofolate Reductase activity	128.9	181.97	ng/ml	1	No
Vancomycin	Cell wall biosynthesis	145400	72550	ng/ml	2	No

The above results demonstrate that induction of an antisense RNA to genes encoding 50S ribosomal subunit proteins results in a selective and highly significant sensitization of cells to antibiotics that inhibit ribosomal function and protein synthesis. The above results further demonstrate that induction of an antisense construct to an essential gene sensitizes an organism to compounds that interfere with that gene products' biological role. This sensitization is restricted to compounds that interfere with pathways associated with the targeted gene and its product.

Assays utilizing antisense constructs to essential genes can be used to identify compounds that specifically interfere with the activity of multiple targets in a pathway. Such constructs can be used to simultaneously screen a sample against multiple targets in one pathway in one reaction (Combinatorial HTS).

Furthermore, as discussed above, panels of antisense construct containing cells may be used to characterize the point of intervention of any compound affecting an essential biological pathway including antibiotics with no known mechanism of action.

Another embodiment of the present invention is a method for determining the pathway against which a test antibiotic compound is active in which the activity of target proteins or nucleic acids involved in proliferation-required pathways is reduced by contacting cells with a sublethal concentration of a known antibiotic which acts against the target protein or nucleic acid. In one embodiment, the target protein or nucleic acid is a target protein or nucleic acid corresponding to a proliferation-required nucleic acid identified using the methods described above. The method is similar to those described above for determining which pathway a test antibiotic acts against except that rather than reducing the activity or level of a proliferation-required gene product using a sublethal level of antisense to a proliferation-required nucleic acid, the activity or level of the proliferation-required gene product is reduced using sublethal level of a known antibiotic which acts against the proliferation required gene product.

Interactions between drugs which affect the same biological pathway has been described in the literature. For example, Mecillinam (Amdinocillin) binds to and inactivates the penicillin binding protein 2 (PBP2, product of the *mrdA* in *E. coli*). This antibiotic interacts with other antibiotics that inhibit PBP2 as well as antibiotics that inhibit other penicillin binding proteins such as PBP3 [(Gutmann, L., Vincent, S., Billot-Klein, D., Acar, J.F., Mrena, E., and Williamson, R. (1986) Involvement of penicillin-binding protein 2 with other penicillin-binding proteins in lysis of *Escherichia coli* by some beta-lactam antibiotics alone and in synergistic lytic effect of amdinocillin (mecillinam). Antimicrobial Agents & Chemotherapy, 30:906-912), the disclosure of which is incorporated herein by reference in its entirety]. Interactions between drugs could, therefore, involve two drugs that inhibit the same target protein or nucleic acid or inhibit different proteins or nucleic acids in the same pathway [(Fukuoka, T., Domon, H., Kakuta, M., Ishii, C., Hirasawa, A., Utsui, Y., Ohya, S., and Yasuda, H. (1997) Combination effect between panipenem and vancomycin on highly methicillin-resistant *Staphylococcus aureus*. Japan. J. Antibio. 50:411-419; Smith, C.E., Foleno, B.E., Barrett, J.F., and Frosc, M.B. (1997) Assessment of the synergistic interactions of levofloxacin and ampicillin against *Enterococcus faecium* by the checkerboard agar dilution and time-kill methods. Diagnos. Microbiol. Infect. Disease 27:85-92; den Hollander, J.G., Horrevorts, A.M., van Goor, M.L.,

Verbrugh, H.A., and Mouton, J.W. (1997) Synergism between tobramycin and ceftazidime against a resistant *Pseudomonas aeruginosa* strain, tested in an in vitro pharmacokinetic model. *Antimicrobial Agents & Chemotherapy*. 41:95-110), the disclosure of all of which are incorporated herein by reference in their entireties].

Two drugs may interact even though they inhibit different targets. For example, the proton pump inhibitor, Omeprazole, and the antibiotic, Amoxycillin, two synergistic compounds acting together, can cure *Helicobacter pylori* infection [( Gabryelewicz, A., Laszewicz, W., Dzieniszewski, J., Ciok, J., Marlicz, K., Bielecki, D., Popiela, T., Legutko, J., Knapik, Z., Poniewierka, E. (1997) Multicenter evaluation of dual-therapy (omeprazol and amoxycillin) for *Helicobacter pylori*-associated duodenal and gastric ulcer (two years of the observation). *J. Physiol. Pharmacol.* 48 Suppl 4:93-105), the disclosure of which is incorporated herein by reference in its entirety].

The growth inhibition from the sublethal concentration of the known antibiotic may be at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, or at least about 75%, or more.

Alternatively, the sublethal concentration of the known antibiotic may be determined by measuring the activity of the target proliferation-required gene product rather than by measuring growth inhibition.

Cells are contacted with a combination of each member of a panel of known antibiotics at a sublethal level and varying concentrations of the test antibiotic. As a control, the cells are contacted with varying concentrations of the test antibiotic alone. The  $IC_{50}$  of the test antibiotic in the presence and absence of the known antibiotic is determined. If the  $IC_{50}$ s in the presence and absence of the known drug are substantially similar, then the test drug and the known drug act on different pathways. If the  $IC_{50}$ s are substantially different, then the test drug and the known drug act on the same pathway.

Another embodiment of the present invention is a method for identifying a candidate compound for use as an antibiotic in which the activity of target proteins or nucleic acids involved in proliferation-required pathways is reduced by contacting cells with a sublethal concentration of a known antibiotic which acts against the target protein or nucleic acid. In one embodiment, the target protein or nucleic acid is a target protein or nucleic acid corresponding to a proliferation-required nucleic acid identified using the methods described above. The method is similar to those described above for identifying candidate compounds for use as antibiotics except that rather than reducing the activity or level of a proliferation-required gene product using a sublethal level of antisense to a proliferation-required nucleic acid, the activity or level of the proliferation-required gene product is reduced using a sublethal level of a known antibiotic which acts against the proliferation required gene product.

The growth inhibition from the sublethal concentration of the known antibiotic may be at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, or at least about 75%, or more.

Alternatively, the sublethal concentration of the known antibiotic may be determined by measuring the activity of the target proliferation-required gene product rather than by measuring growth inhibition.

In order to characterize test compounds of interest, cells are contacted with a panel of known antibiotics at a sublethal level and one or more concentrations of the test compound. As a control, the cells are contacted with the same concentrations of the test compound alone. The  $IC_{50}$  of the test compound in the presence and absence of the known antibiotic is determined. If the  $IC_{50}$  of the test compound is substantially different in the presence and absence of the known drug then the test compound is a good candidate for use as an antibiotic. As discussed above, once a candidate compound is identified using the above methods its structure may be optimized using standard techniques such as combinatorial chemistry.

Representative known antibiotics which may be used in each of the above methods are provided in the table below. However, it will be appreciated that other antibiotics may also be used.

ANTIBIOTIC	INHIBITS/TARGET	RESISTANT MUTANTS
<b>Inhibitors of Transcription</b>		
Rifamycin, 1959 Rifampicin	Inhibits initiation of transcription/ $\beta$ -subunit RNA polymerase, <i>rpoB</i>	<i>rpoB</i> , <i>crp</i> , <i>cyaA</i>
Rifabutin Rifaximin		
Streptolydigin	Accelerates transcription chain termination/ $\beta$ -subunit RNA polymerase	<i>rpoB</i>
Streptovaricin	an acyclic ansamycin, inhibits RNA polymerase	<i>rpoB</i>
Actinomycin D + EDTA	Intercalates between 2 successive G-C pairs, <i>rpoB</i> , inhibits RNA synthesis	<i>pldA</i>
<b>Inhibitors of Nucleic Acid Metabolism</b>		
Quinolones, 1962 Nalidixic acid	subunit gyrase and/or topoisomerase IV, <i>gyrA</i>	
Oxolinic acid		<i>gyrA</i> or <i>B</i> , <i>icd</i> , <i>sloB</i>
Fluoroquinolones Ciprofloxacin, 1983 Norfloxacin	subunit gyrase, <i>gyrA</i> and/or topoisomerase IV (probable target in Staph)	<i>gyrA</i> <i>norA</i> (efflux in Staph) <i>hipQ</i>
Coumerins Novobiocin	Inhibits ATPase activity of $\beta$ -subunit gyrase, <i>gyrB</i>	<i>gyrB</i> , <i>cysB</i> , <i>cysE</i> , <i>nov</i> , <i>ompA</i>
Coumermycin	Inhibits ATPase activity of $\beta$ -subunit gyrase, <i>gyrB</i>	<i>gyrB</i> , <i>hisW</i>
Albicidin	DNA synthesis	<i>tsx</i> (nucleoside channel)
Metronidazole	Causes single-strand breaks in DNA	<i>nar</i>
<b>Inhibitors of Metabolic Pathways</b>		
Sulfonamides, 1932 Sulfanilamide	blocks synthesis of dihydrofolate, dihydro- pteroate synthesis, <i>folP</i>	<i>folP</i> , <i>gpt</i> , <i>pabA</i> , <i>pabB</i> , <i>pabC</i>
Trimethoprim, 1962	Inhibits dihydrofolate reductase, <i>folA</i>	<i>folA</i> , <i>thyA</i>
Showdomycin	Nucleoside analogue capable of alkylating	<i>nupC</i> , <i>pnp</i>

ANTIBIOTIC	INHIBITS/TARGET	RESISTANT MUTANTS
Thiolactomycin	sulfhydryl groups, inhibitor of thymidylate synthetase type II fatty acid synthase inhibitor	<i>emrB</i> <i>fadB</i> , <i>emrB</i> due to gene dosage <i>guaA,B</i>
Psicofuranine	Adenosine glycoside antibiotic, target is GMP synthetase	<i>fabI (envM)</i> <i>fabI (envM)</i>
Triclosan	Inhibits fatty acid synthesis	
Diazaborines Isoniazid, Ethionamide	heterocyclic, contains boron, inhibit fatty acid synthesis, enoyl-ACP reductase, <i>fabI</i>	
<b>Inhibitors of Translation</b>		
Phenylpropanoids Chloramphenicol, 1947	Binds to ribosomal peptidyl transfer center preventing peptide translocation/ binds to S6, L3, L6, L14, L16, L25, L26, L27, but preferentially to L16	<i>rrn</i> , <i>cmlA</i> , <i>marA</i> , <i>ompF</i> , <i>ompR</i>
Tetracyclines, 1948, type II polyketides Minocycline Doxycycline	Binding to 30S ribosomal subunit, "A" site on 30S subunit, blocks peptide elongation, strongest binding to S7	<i>clmA (cmr)</i> , <i>mar</i> , <i>ompF</i>
Macrolides (type I polyketides) Erythromycin, 1950 Carbomycin, Spiramycin	Binding to 50 S ribosomal subunit, 23S rRNA, blocks peptide translocation, L15, L4, L12	<i>rrn</i> , <i>rplC</i> , <i>rplD</i> , <i>rplV</i> , <i>mac</i>
etc		
Aminoglycosides Streptomycin, 1944 Neomycin	Irreversible binding to 30S ribosomal subunit, prevents translation or causes mistranslation of mRNA/16S rRNA	<i>rpsL</i> , <i>strC,M</i> , <i>ubiF</i> <i>atpA-E</i> , <i>ecfB</i> , <i>hemAC,D,E,G</i> , <i>topA</i> , <i>rpsC,D,E</i> , <i>rrn</i> , <i>spcB</i> <i>atpA-atpE</i> , <i>cpxA</i> , <i>ecfB</i> , <i>hemA,B,L</i> , <i>topA</i> <i>ksgA,B,C,D</i> , <i>rplB,K</i> , <i>rpsI,N,M,R</i> <i>rplF</i> , <i>ubiF</i> <i>cpxA</i> <i>rpsL</i>
Spectinomycin Kanamycin		
Kasugamycin		
Gentamicin, 1963 Amikacin Paromycin		
Lincosamides Lincomycin, 1955 Clindamycin	Binding to 50 S ribosomal subunit, blocks peptide translocation	<i>linB</i> , <i>rplN,O</i> , <i>rpsG</i>
Streptogramins Virginiamycin, 1955 Pristinamycin	2 components, Streptogramins A&B, bind to the 50S ribosomal subunit blocking peptide translocation and peptide bond formation	
Synergid: quinupristin /dalfopristin		
Fusidanes Fusidic Acid	Inhibition of elongation factor G (EF-G) prevents peptide translocation	<i>fusA</i>
Kirromycin (Mocimycin)	Inhibition of elongation factor TU (EF-Tu), prevents peptide bond formation	<i>tufA,B</i>

ANTIBIOTIC	INHIBITS/TARGET	RESISTANT MUTANTS
Pulvomycin	Binds to and inhibits EF-TU	
Thiopeptin	Sulfur-containing antibiotic, inhibits protein synthesis, EF-G	<i>rplE</i>
Tiamulin	Inhibits protein synthesis	<i>rplC, rplD</i>
Negamycin	Inhibits termination process of protein synthesis	<i>prfB</i>
Oxazolidinones Linezolid	23S rRNA	
Isoniazid		<i>pdx</i>
Nitrofurantoin	Inhibits protein synthesis, nitroreductases convert nitrofurantoin to highly reactive electrophilic intermediates which attack bacterial ribosomal proteins non-specifically	<i>nfnA, B</i>
Pseudomonic Acids Mupirocin (Bactroban)	Inhibition of isoleucyl tRNA synthetase-used for Staph, topical cream, nasal spray	<i>ileS</i>
Indolmycin	Inhibits tryptophanyl-tRNA synthetase	<i>trpS</i>
Viomycin		<i>rrmA</i> (23S rRNA methyltransferase; mutant has slow growth rate, slow chain elongation rate, and viomycin resistance)
Thiopeptides	Binds to L11-23S RNA complex	
Thiostrepton	Inhibits GTP hydrolysis by EF-G	
Micrococcin	Stimulates GTP hydrolysis by EF-G	
<b>Inhibitors of Cell Walls/Membranes</b>		
<b><math>\beta</math>-lactams</b>		
Penicillin, 1929 Ampicillin	Inhibition of one or more cell wall transpeptidases, endopeptidases, and glycosidases (PBPs), of the 12 PBPs only 2 are essential: <i>mrdA</i> (PBP2) and <i>ftsI</i> ( <i>pbpB</i> , PBP3)	<i>ampC, ampD, ampE, envZ, galU, hipA, hipQ, ompC, ompF, ompR, ptsI, rfa, tolD, tolE</i>
Methicillin, 1960		
<b>Cephalosporins, 1962</b>		
Mecillinam (amdinocillin)	Binds to and inactivates PBP2 ( <i>mrdA</i> ) Inactivates PBP3 ( <i>ftsI</i> )	<i>tonB</i> <i>alaS, argS, crp, cyaA, envB, mrdA, B, mreB, C, D</i>
Aztreonam (Furazlocillin)		
Bacilysin, Tetaine	Dipeptide, inhib glucosamine synthase	<i>dppA</i>
Glycopeptides Vancomycin, 1955	Inhib G+ cell wall syn, binds to terminal D-alanyl-D-alanine of pentapeptide,	
Polypeptides Bacitracin	Prevents dephosphorylation and regeneration of lipid carrier	<i>rfa</i>
Cyclic lipopeptide Daptomycin, 1980	Disrupts multiple aspects of membrane	



	function, including peptidoglycan synthesis, lipoteichoic acid synthesis, and the bacterial membrane potential	
Cyclic polypeptides Polymixin, 1939	Surfactant action disrupts cell membrane lipids, binds lipid A moiety of LPS	<i>pmrA</i>
Fosfomycin, 1969	Analogue of P-enolpyruvate, inhibits 1 <sup>st</sup> step in peptidoglycan synthesis - UDP-N-acetylglucosamine enolpyruvyl transferase, <i>murA</i> . Also acts as Immunosuppressant	<i>murA, crp, cyaA glpT, hipA, ptsI, uhpT</i>
Cycloserine	Prevents formation of D-ala dimer, inhibits D-ala ligase, <i>ddlA, B</i>	<i>hipA, cycA</i>
Alafosfalin	phosphonodipeptide, cell wall synthesis inhibitor, potentiator of $\beta$ -lactams	<i>pepA, tpp</i>
<b>Inhibitors of Protein Processing/Transport</b>		
Globomycin	Inhibits signal peptidase II (cleaves prolipoproteins subsequent to lipid modification, <i>lspA</i> )	<i>lpp, dnaE</i>

## EXAMPLE 12

Transfer of Exogenous Nucleic Acid Sequences to other Bacterial Species Using the *E. coli* Expression Vectors or Expression Vectors Functional in Bacterial Species other than *E. coli*.

5 The above methods were validated using antisense nucleic acids which inhibit the growth of *E. coli* which were identified using methods similar to those described above. Expression vectors which inhibited growth of *E. coli* upon induction of antisense RNA expression with IPTG were transformed directly into *Enterobacter cloacae*, *Klebsiella pneumonia* or *Salmonella typhimurium*. The transformed cells were then assayed for growth inhibition according to the method of Example 1. After growth in liquid culture, cells were plated at various serial dilutions and a score determined by calculating the log difference in growth for INDUCED vs. UNINDUCED antisense RNA expression as determined by the maximum 10 fold dilution at which a colony was observed. The results of these experiments are listed below in Table VI. If there was no effect of antisense RNA expression in an organism, the clone is minus in Table VI. In contrast, a positive in Table VI means that at least 10 fold more cells were required to observe a colony on the induced plate than on the non-induced plate under the conditions used and in that organism.

15 Sixteen of the constructs were found to inhibit growth in all the organisms tested upon induction of antisense RNA expression with IPTG. Those skilled in the art will appreciate that a negative result in a heterologous organism does not mean that that organism is missing that gene nor does it mean that the gene is unessential. However, a positive result means that the heterologous organism contains a homologous gene which is required for proliferation of that organism. The homologous gene may be obtained using the methods described herein. Those cells that are inhibited by antisense may be used in cell based assays as described herein for the identification and characterization of compounds in order to

develop antibiotics effective in these organisms. Those skilled in the art will appreciate that an antisense molecule which works in the organism from which it was obtained will not always work in a heterologous organism.

TABLE VI

Sensitivity of Other Microorganisms to Antisense Nucleic Acids That Inhibit Proliferation in *E. coli*

Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA001	+	+	-
EcXA004	-	-	-
EcXA005	+	+	+
EcXA006	-	-	-
EcXA007	-	+	-
EcXA008	+	-	+
EcXA010	+	+	+
EcXA011	-	+	-
EcXA012	-	+	-
EcXA013	+	+	+
EcXA014	+	+	-
EcXA015	-	+	+
EcXA016	+	+	+
EcXA017	+	+	+
EcXA018	+	+	+
EcXA019	+	+	+
EcXA020	+	+	+
EcXA021	+	+	+
EcXA023	+	+	+
EcXA024	+	-	+
EcXA025	-	-	-
EcXA026	+	+	-
EcXA027	+	+	+
EcXA028	+	-	-
EcXA029	-	-	-

Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA030	+	+	+
EcXA031	+	.	.
EcXA032	+	.	.
EcXA033	+	+	+
EcXA034	+	+	+
EcXA035	.	.	.
EcXA036	+	.	+
EcXA037	.	+	.
EcXA038	+	+	.
EcXA039	+	.	.
EcXA041	+	+	+
EcXA042	.	+	+
EcXA044	.	.	.
EcXA045	.	+	.
EcXA046	.	.	.
EcXA047	+	+	.
EcXA048	.	.	.
EcXA049	+	.	.
EcXA050	.	.	.
EcXA051	+	.	.
EcXA052	+	.	.
EcXA053	+	+	+
EcXA054	.	.	+
EcXA055	+	.	.

## EXAMPLE 13

Use of Identified Exogenous Nucleic Acid Sequences as Probes

5

The identified sequence of the present invention can be used as probes to obtain the sequence of additional genes of interest from a second organism. For example, probes to potential bacterial target proteins may be hybridized to nucleic acids from other organisms including other bacteria and higher organisms, to identify homologous sequences. Such

hybridization might indicate that the protein encoded by the gene to which the probe corresponds is found in humans and therefore not necessarily a good drug target. Alternatively, the gene can be conserved only in bacteria and therefore would be a good drug target for a broad spectrum antibiotic or antimicrobial.

Probes derived from the identified nucleic acid sequences of interest or portions thereof can be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe can be single stranded or double stranded and can be made using techniques known in the art, including *in vitro* transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it can be denatured prior to contacting the probe. In some applications, the nucleic acid sample can be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample can comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe can be cloned into vectors such as expression vectors, sequencing vectors, or *in vitro* transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques can be used to isolate, purify and clone sequences from a genomic library, made from a variety of bacterial species, which are capable of hybridizing to probes made from the sequences identified in Examples 5 and 6.

#### EXAMPLE 14

##### Preparation of PCR Primers and Amplification of DNA

The identified *E. coli* genes corresponding directly to or located within the operon of nucleic acid sequences required for proliferation or portions thereof can be used to prepare PCR primers for a variety of applications, including the identification or isolation of homologous sequences from other species, for example *S. typhimurium*, *E. cloacae*, and *Klebsiella pneumoniae*, which contain part or all of the homologous genes. Because homologous genes are related but not identical in sequence, those skilled in the art will often employ degenerate sequence PCR primers. Such degenerate sequence primers are designed based on conserved sequence regions, either known or suspected, such as conserved coding regions. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. The PCR primers are at least 10 bases, and preferably at least 20 bases in length. More preferably, the PCR primers are at least 20-30 bases in length. In some embodiments, the PCR primers can be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering White, B.A. Ed. in *Methods in Molecular Biology* 67: Humana Press, Totowa 1997. When the entire coding sequence of the target gene is known, the 5' and 3' regions of the target gene

can be used as the sequence source for PCR probe generation. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

#### EXAMPLE 15

##### Inverse PCR

The technique of inverse polymerase chain reaction can be used to extend the known nucleic acid sequence identified in Examples 5 and 6. The inverse PCR reaction is described generally by Ochman et al., in Ch. 10 of **PCR Technology: Principles and Applications for DNA Amplification**, (Henry A. Erlich, Ed.) W.H. Freeman and Co. (1992). Traditional PCR requires two primers that are used to prime the synthesis of complementary strands of DNA. In inverse PCR, only a core sequence need be known.

Using the sequences identified as relevant from the techniques taught in Examples 5 and 6 and applied to other species of bacteria, a subset of exogenous nucleic sequences are identified that correspond to genes or operons that are required for bacterial proliferation. In species for which a genome sequence is not known, the technique of inverse PCR provides a method for obtaining the gene in order to determine the sequence or to place the probe sequences in full context to the target sequence to which the identified exogenous nucleic acid sequence binds.

To practice this technique, the genome of the target organism is digested with an appropriate restriction enzyme so as to create fragments of nucleic acid that contain the identified sequence as well as unknown sequences that flank the identified sequence. These fragments are then circularized and become the template for the PCR reaction. PCR primers are designed in accordance with the teachings of Example 15 and directed to the ends of the identified sequence are synthesized. The primers direct nucleic acid synthesis away from the known sequence and toward the unknown sequence contained within the circularized template. After the PCR reaction is complete, the resulting PCR products can be sequenced so as to extend the sequence of the identified gene past the core sequence of the identified exogenous nucleic acid sequence identified. In this manner, the full sequence of each novel gene can be identified. Additionally the sequences of adjacent coding and noncoding regions can be identified.

#### EXAMPLE 16

##### Identification of Genes Required for *Staphylococcus aureus* Proliferation

Genes required for proliferation in *Staphylococcus aureus* are identified according to the methods described above.

#### EXAMPLE 17

##### Identification of Genes Required for *Neisseria gonorrhoeae* Proliferation

Genes required for proliferation in *Neisseria gonorrhoeae* are identified according to the methods described above.

**EXAMPLE 18**Identification of Genes Required for *Pseudomonas aeruginosa* Proliferation

Genes required for proliferation in *Pseudomonas aeruginosa* are identified according to the methods described above.

**EXAMPLE 19**Identification of Genes Required for *Enterococcus faecalis* Proliferation

Genes required for proliferation in *Enterococcus faecalis* are identified according to the methods described above.

**EXAMPLE 20**Identification of Genes Required for *Haemophilus influenzae* Proliferation

Genes required for proliferation in *Haemophilus influenzae* are identified according to the methods described above.

**EXAMPLE 21**Identification of Genes Required for *Salmonella typhimurium* Proliferation

Genes required for proliferation in *Salmonella typhimurium* are identified according to the methods described above.

**EXAMPLE 22**Identification of Genes Required for *Helicobacter pylori* Proliferation

Genes required for proliferation in *Helicobacter pylori* are identified according to the methods described above.

**EXAMPLE 23**Identification of Genes Required for *Mycoplasma pneumoniae* Proliferation

Genes required for proliferation in *Mycoplasma pneumoniae* are identified according to the methods described above.

**EXAMPLE 24**Identification of Genes Required for *Plasmodium ovale* Proliferation

Genes required for proliferation in *Plasmodium ovale* are identified according to the methods described above.

**EXAMPLE 25**Identification of Genes Required for *Saccharomyces cerevisiae* Proliferation

Genes required for proliferation in *Saccharomyces cerevisiae* are identified according to the methods described above.

**EXAMPLE 26**Identification of Genes Required for *Entamoeba histolytica* Proliferation

Genes required for proliferation in *Entamoeba histolytica* are identified according to the methods described above.

**EXAMPLE 27**Identification of Genes Required for *Candida albicans* Proliferation

Genes required for proliferation in *Candida albicans* are identified according to the methods described above.

**EXAMPLE 28**Identification of Genes Required for *Klebsiella pneumoniae* Proliferation

Genes required for proliferation in *Klebsiella pneumoniae* are identified according to the methods described above.

**EXAMPLE 29**Identification of Genes Required for *Salmonella typhi* Proliferation

Genes required for proliferation in *Salmonella typhi* are identified according to the methods described above.

**EXAMPLE 30**Identification of Genes Required for *Salmonella paratyphi* Proliferation

Genes required for proliferation in *Salmonella paratyphi* are identified according to the methods described above.

**EXAMPLE 31**Identification of Genes Required for *Salmonella choleraesuis* Proliferation

Genes required for proliferation in *Salmonella choleraesuis* are identified according to the methods described above.

**EXAMPLE 32**Identification of Genes Required for *Staphylococcus epidermis* Proliferation

Genes required for proliferation in *Staphylococcus epidermis* are identified according to the methods described above.

**EXAMPLE 33**Identification of Genes Required for *Mycobacterium tuberculosis* Proliferation

Genes required for proliferation in *Mycobacterium tuberculosis* are identified according to the methods described above.

**EXAMPLE 34**Identification of Genes Required for *Mycobacterium leprae* Proliferation

Genes required for proliferation in *Mycobacterium leprae* are identified according to the methods described above.

**EXAMPLE 35**Identification of Genes Required for *Treponema pallidum* Proliferation

Genes required for proliferation in *Treponema pallidum* are identified according to the methods described above.

**EXAMPLE 36**Identification of Genes Required for *Bacillus anthracis* Proliferation

Genes required for proliferation in *Bacillus anthracis* are identified according to the methods described above.

**EXAMPLE 37**Identification of Genes Required for *Yersinia pestis* Proliferation

Genes required for proliferation in *Yersinia pestis* are identified according to the methods described above.

**EXAMPLE 38**Identification of Genes Required for *Clostridium botulinum* Proliferation

Genes required for proliferation in *Clostridium botulinum* are identified according to the methods described above.

**EXAMPLE 39**Identification of Genes Required for *Campylobacter jejuni* Proliferation

Genes required for proliferation in *Campylobacter jejuni* are identified according to the methods described above.

**EXAMPLE 40**Identification of Genes Required for *Chlamydia trachomatis* Proliferation

Genes required for proliferation in *Chlamydia trachomatis* are identified according to the methods described above.

**Use of Isolated Exogenous Nucleic Acid Fragments as Antisense Antibiotics**

In addition to using the identified sequences to enable screening of molecule libraries to identify compounds useful to identify antibiotics, the sequences themselves can be used as therapeutic agents. Specifically, the identified exogenous sequences in an antisense orientation can be provided to an individual to inhibit the translation of a bacterial target gene.

Generation of Antisense Therapeutics from Identified Exogenous Sequences

The sequences of the present invention can be used as antisense therapeutics for the treatment of bacterial infections or simply for inhibition of bacterial growth *in vitro* or *in vivo*. The therapy exploits the biological process in cells where genes are transcribed into messenger RNA (mRNA) that is then translated into proteins. Antisense RNA technology contemplates the use of antisense oligonucleotides directed against a target gene that will bind to its target and decrease or inhibit the translation of the target mRNA. In one embodiment, antisense oligonucleotides can be used to treat and control a bacterial infection of a cell culture containing a population of desired cells contaminated with bacteria. In another embodiment, the antisense oligonucleotides can be used to treat an organism with a bacterial infection.

Antisense oligonucleotides can be synthesized from any of the sequences of the present invention using methods well known in the art. In a preferred embodiment, antisense oligonucleotides are synthesized using artificial means. Uhlmann & Peymann, Chemical Rev. 90:543-584 (1990) review antisense oligonucleotide technology in detail. Modified or unmodified antisense oligonucleotides can be used as therapeutic agents. Modified antisense oligonucleotides are preferred since it is well known that antisense oligonucleotides are extremely unstable. Modification of the phosphate backbones of the antisense oligonucleotides can be achieved by substituting the internucleotide phosphate residues with methylphosphonates, phosphorothioates, phosphoramidates, and phosphate esters. Nonphosphate internucleotide analogs such as siloxane bridges, carbonate bridges, thioester bridges, as well as many others known in the art. The preparation of certain antisense oligonucleotides with modified internucleotide linkages is described in U.S. Patent No. 5,142,047, hereby incorporated by reference.

Modifications to the nucleoside units of the antisense oligonucleotides are also contemplated. These modifications can increase the half-life and increase cellular rates of uptake for the oligonucleotides *in vivo*. For example,



$\alpha$ -anomeric nucleotide units and modified bases such as 1,2-dideoxy-d-ribofuranose, 1,2-dideoxy-1-phenylribofuranose, and *N*, *N*-ethano-5-methyl-cytosine are contemplated for use in the present invention.

An additional form of modified antisense molecules is found in peptide nucleic acids. Peptide nucleic acids (PNA) have been developed to hybridize to single and double stranded nucleic acids. PNA are nucleic acid analogs in which the entire deoxyribose-phosphate backbone has been exchanged with a chemically completely different, but structurally homologous, polyamide (peptide) backbone containing 2-aminoethyl glycine units. Unlike DNA, which is highly negatively charged, the PNA backbone is neutral. Therefore, there is much less repulsive energy between complementary strands in a PNA-DNA hybrid than in the comparable DNA-DNA hybrid, and consequently they are much more stable. PNA can hybridize to DNA in either a Watson/Crick or Hoogsteen fashion (Demidov et al., *Proc. Natl. Acad. Sci. U.S.A.* 92:2637-2641, 1995; Egholm, *Nature* 365:566-568, 1993; Nielsen et al., *Science* 254:1497-1500, 1991; Dueholm et al., *New J. Chem.* 21:19-31, 1997).

Molecules called PNA "clamps" have been synthesized which have two identical PNA sequences joined by a flexible hairpin linker containing three 8-amino-3,6-dioxaoctanoic acid units. When a PNA clamp is mixed with a complementary homopurine or homopyrimidine DNA target sequence, a PNA-DNA-PNA triplex hybrid can form which has been shown to be extremely stable (Bentin et al., *Biochemistry* 35:8863-8869, 1996; Egholm et al., *Nucleic Acids Res.* 23:217-222, 1995; Griffith et al., *J. Am. Chem. Soc.* 117:831-832, 1995).

The sequence-specific and high affinity duplex and triplex binding of PNA have been extensively described (Nielsen et al., *Science* 254:1497-1500, 1991; Egholm et al., *J. Am. Chem. Soc.* 114:9677-9678, 1992; Egholm et al., *Nature* 365:566-568, 1993; Almarsson et al., *Proc. Natl. Acad. Sci. U.S.A.* 90:9542-9546, 1993; Demidov et al., *Proc. Natl. Acad. Sci. U.S.A.* 92:2637-2641, 1995). They have also been shown to be resistant to nuclease and protease digestion (Demidov et al., *Biochem. Pharm.* 48:1010-1313, 1994). PNA has been used to inhibit gene expression (Hanvey et al., *Science* 258:1481-1485, 1992; Nielsen et al., *Nucl. Acids. Res.*, 21:197-200, 1993; Nielsen et al., *Gene* 149:139-145, 1994; Good & Nielsen, *Science*, 95: 2073-2076, 1998; all of which are hereby incorporated by reference), to block restriction enzyme activity (Nielsen et al., *supra.*, 1993), to act as an artificial transcription promoter (Mollegaard, *Proc. Natl. Acad. Sci. U.S.A.* 91:3892-3895, 1994) and as a pseudo restriction endonuclease (Demidov et al., *Nucl. Acids. Res.* 21:2103-2107, 1993). Recently, PNA has also been shown to have antiviral and antitumoral activity mediated through an antisense mechanism (Norton, *Nature Biotechnol.*, 14:615-619, 1996; Hirschman et al., *J. Investig. Med.* 44:347-351, 1996). PNAs have been linked to various peptides in order to promote PNA entry into cells (Basu et al., *Bioconj. Chem.* 8:481-488, 1997; Pardridge et al., *Proc. Natl. Acad. Sci. U.S.A.* 92:5592-5596, 1995).

The antisense oligonucleotides contemplated by the present invention can be administered by direct application of oligonucleotides to a target using standard techniques well known in the art. The antisense oligonucleotides can be generated within the target using a plasmid, or a phage. Alternatively, the antisense nucleic acid may be expressed from a sequence in the chromosome of the target cell. It is further contemplated that contemplated that the antisense oligonucleotide contemplated are incorporated in a ribozyme sequence to enable the antisense to specifically bind and cleave its

target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., *Pharmacol. Ther.* 50(2):245-254, (1991), which is hereby incorporated by reference. The present invention also contemplates using a retron to introduce an antisense oligonucleotide to a cell. Retron technology is exemplified by U.S. Patent No. 5,405,775, which is hereby incorporated by reference. Antisense oligonucleotides can also be delivered using liposomes or by electroporation techniques which are well known in the art.

The antisense nucleic acids of the present invention can also be used to design antibiotic compounds comprising nucleic acids which function by intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. The sequences identified as required for proliferation in the present invention, or portions thereof, can be used as templates to inhibit microorganism gene expression in individuals infected with such organisms. Traditionally, homopurine sequences were considered the most useful for triple helix strategies. However, homopyrimidine sequences can also inhibit gene expression. Such homopyrimidine oligonucleotides bind to the major groove at homopurine:homopyrimidine sequences. Thus, both types of sequences based on the sequences of the present invention that are required for proliferation are contemplated for use as antibiotic compound templates.

The antisense oligonucleotides of this example employ the identified sequences of the present invention to induce bacterial cell death or at least bacterial stasis by inhibiting target gene translation. Antisense oligonucleotides containing from about 8 to 40 bases of the sequences of the present invention have sufficient complementarity to form a duplex with the target sequence under physiological conditions.

To kill bacterial cells or inhibit their growth, the antisense oligonucleotides are applied to the bacteria or to the target cells under conditions that facilitate their uptake. These conditions include sufficient incubation times of cells and oligonucleotides so that the antisense oligonucleotides are taken up by the cells. In one embodiment, an incubation period of 7-10 days is sufficient to kill bacteria in a sample. An optimum concentration of antisense oligonucleotides is selected for use.

The concentration of antisense oligonucleotides to be used can vary depending on the type of bacteria sought to be controlled, the nature of the antisense oligonucleotide to be used, and the relative toxicity of the antisense oligonucleotide to the desired cells in the treated culture. Antisense oligonucleotides can be introduced to cell samples at a number of different concentrations preferably between  $1 \times 10^{-10}$  M to  $1 \times 10^{-4}$  M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use *in vivo*. For example, an inhibiting concentration in culture of  $1 \times 10^{-7}$  translates into a dose of approximately 0.6 mg/kg body weight. Levels of oligonucleotide approaching 100 mg/kg body weight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the subject are removed, treated with the antisense oligonucleotide, and reintroduced into the subject. This range is merely illustrative and one of skill in the art are able to determine the optimal concentration to be used in a given case.

After the bacterial cells have been killed or controlled in a desired culture, the desired cell population may be used for other purposes.

#### EXAMPLE 41

5 The following example demonstrates the ability of an *E. coli* antisense oligonucleotide to act as a bactericidal or bacteriostatic agent to treat a contaminated cell culture system. The application of the antisense oligonucleotides of the present invention are thought to inhibit the translation of bacterial gene products required for proliferation.

10 The antisense oligonucleotide of this example corresponds to a 30 base phosphorothioate modified oligodeoxynucleotide complementary to a nucleic acid involved in proliferation, such as Molecule Number EcXA001. A sense oligodeoxynucleotide complementary to the antisense sequence is synthesized and used as a control. The oligonucleotides are synthesized and purified according to the procedures of Matsukura, et al., Gene 72:343 (1988). The test oligonucleotides are dissolved in a small volume of autoclaved water and added to culture medium to make a 100 micromolar stock solution.

15 Human bone marrow cells are obtained from the peripheral blood of two patients and cultured according standard procedures well known in the art. The culture is contaminated with the K-12 strain of *E. coli* and incubated at 37°C overnight to establish bacterial infection.

20 The control and antisense oligonucleotide containing solutions are added to the contaminated cultures and monitored for bacterial growth. After a 10 hour incubation of culture and oligonucleotides, samples from the control and experimental cultures are drawn and analyzed for the translation of the target bacterial gene using standard microbiological techniques well known in the art. The target *E. coli* gene is found to be translated in the control culture treated with the control oligonucleotide, however, translation of the target gene in the experimental culture treated with the antisense oligonucleotide of the present invention is not detected or reduced.

#### EXAMPLE 42

25 A subject suffering from an *E. coli* infection is treated with the antisense oligonucleotide preparation of Example 39. The antisense oligonucleotide is provided in a pharmaceutically acceptable carrier at a concentration effective to inhibit the translation of the target gene. The present subject is treated with a concentration of antisense oligonucleotide sufficient to achieve a blood concentration of about 100 micromolar. The patient receives daily injections of antisense oligonucleotide to maintain this concentration for a period of 1 week. At the end of the week a blood sample is drawn and analyzed for the presence or absence using standard techniques well known in the art. There is no detectable evidence of *E. coli* and the treatment is terminated.

#### EXAMPLE 43

##### Preparation and use of Triple Helix Probes

30 The sequences of microorganism genes required for proliferation of the present invention are scanned to identify 10-mer to 20-mer homopyrimidine or homopurine stretches that could be used in triple-helix based strategies for inhibiting gene

expression. Following identification of candidate homopyrimidine or homopurine stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into a population of bacterial cells that normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

The oligonucleotides can be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for a reduction in proliferation using techniques such as monitoring growth levels as compared to untreated cells using optical density measurements. The oligonucleotides that are effective in inhibiting gene expression in cultured cells can then be introduced *in vivo* using the techniques well known in that art at a dosage level shown to be effective.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the generation of oligonucleotides suitable for triple helix formation see Griffin et al. (*Science* 245:967-971 (1989), which is hereby incorporated by this reference).

#### EXAMPLE 44

##### Identification of Bacterial Strains from Isolated Specimens by PCR

Classical bacteriological methods for the detection of various bacterial species are time consuming and costly. These methods include growing the bacteria isolated from a subject in specialized media, cultivation on selective agar media, followed by a set of confirmation assays that can take from 8 to 10 days or longer to complete. Use of the identified sequences of the present invention provides a method to dramatically reduce the time necessary to detect and identify specific bacterial species present in a sample.

In one exemplary method, bacteria are grown in enriched media and DNA samples are isolated from specimens of, for example, blood, urine, stool, saliva or central nervous system fluid by conventional methods. A panel of PCR primers based on identified sequences unique to various species of microorganisms are then utilized in accordance with Example 12 to amplify DNA of approximately 100-200 bases in length from the specimen. A separate PCR reaction is set up for each pair of PCR primers and after the PCR reaction is complete, the reaction mixtures are assayed for the presence of PCR product. The presence or absence of bacteria from the species to which the PCR primer pairs belong is determined by the presence or absence of a PCR product in the various test PCR reaction tubes.

Although the PCR reaction is used to assay the isolated sample for the presence of various bacterial species, other assays such as the Southern blot hybridization are also contemplated.

WHAT IS CLAIMED IS:

1. A purified or isolated nucleic acid sequence consisting essentially of one of SEQ ID NOs: 405-485, wherein said nucleic acid inhibits microorganism proliferation.
2. The nucleic acid sequence of Claim 1, wherein said nucleic acid sequence is complementary to at least a portion of a coding sequence of a gene whose expression is required for microorganism proliferation.
3. The nucleic acid sequence of Claims 1 or 2, wherein said nucleic acid comprises a fragment of one of SEQ ID NOs. 405-485, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.
4. The nucleic acid sequence of Claim 3, wherein said nucleic acid sequence is complementary to a coding sequence of a gene whose expression is required for microorganism proliferation.
5. A vector comprising a promoter operably linked to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 405-485.
6. The vector of Claim 5, wherein said promoter is active in an organism selected from the group consisting of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.
7. A host cell containing the vector of Claim 5 or Claim 6.
8. A purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 82-88, 90-242.
9. A fragment of the nucleic acid of Claim 8, said fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.
10. A vector comprising a promoter operably linked to the nucleic acid of Claim 8 or Claim 9.
11. A purified or isolated nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.
12. A purified or isolated nucleic acid comprising a nucleic acid having at least 70% homology to a sequence selected from the group consisting of SEQ ID NOs 405-485, 82-88, 90-242 or the sequences complementary thereto as determined using BLASTN version 2.0 with the default parameters.

13. The nucleic acid of Claim 12, wherein said nucleic acid is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

14. A purified or isolated nucleic acid consisting essentially of a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

15. A vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

16. A host cell containing the vector of Claim 15.

17. A purified or isolated polypeptide comprising the sequence of one of SEQ ID NOs.: 243-357, 359-398.

18. A purified or isolated polypeptide comprising a fragment of one of the polypeptides of SEQ ID NOs. 243-357, 359-398, said fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the polypeptides of SEQ ID NOs.: 243-357, 359-398.

19. An antibody capable of specifically binding the polypeptide of Claim 17 or Claim 18.

20. A method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 into a cell.

21. The method of Claim 20, further comprising the step of isolating said protein.

22. A method of inhibiting proliferation comprising inhibiting the activity or reducing the amount of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

23. A method for identifying compounds which influence the activity of a polypeptide required for proliferation comprising:

contacting a polypeptide having a sequence selected from the group consisting of 243-357, 359-398 with a candidate compound; and

determining whether said compound influences the activity of said polypeptide.

24. The method of Claim 23, wherein said activity is an enzymatic activity.

25. The method of Claim 23, wherein said activity is a carbon compound catabolism activity.

26. The method of Claim 23, wherein said activity is a biosynthetic activity.
27. The method of Claim 23, wherein said activity is a transporter activity.
28. The method of Claim 23, wherein said activity is a transcriptional activity.
29. The method of Claim 23, wherein said activity is a DNA replication activity.
- 5 30. The method of Claim 23, wherein said activity is a cell division activity.
31. A method for assaying compounds for the ability to reduce the activity or level of a polypeptide required for proliferation, comprising:

providing a target, wherein said target comprises the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 82-88, 90-242;

10 contacting said target with a candidate compound; and  
measuring an activity of said target.

32. The method of Claim 31, wherein said target is a messenger RNA molecule transcribed from a coding region of one of SEQ ID. NOs.: 82-88, 90-242 and said activity is translation of said messenger RNA.

15 33. The method of Claim 32, wherein said target is a coding region of one of SEQ ID. NOs. 82-88, 90-242 and said activity is transcription of said messenger RNA.

34. A compound identified using the method of Claim 31.

35. A method for identifying compounds which reduce the activity or level of a gene product required for cell proliferation comprising the steps of:

20 expressing an antisense nucleic acid against a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

contacting said sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

25 36. The method of Claim 35, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

37. The method of Claim 36, wherein said cell is an *E. coli* cell.

30 38. The method of Claim 36, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

39. The method of Claim 35, wherein said antisense nucleic acid is transcribed from an inducible promoter.
40. The method of Claim 39, further comprising the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sublethal level.
41. The method of Claim 40, wherein said sub-lethal concentration of said inducer is such that growth inhibition is 8% or more.
42. The method of Claim 40, wherein said inducer is isopropyl-1-thio- $\beta$ -D-galactoside.
43. The method of Claim 35, wherein growth inhibition is measured by monitoring optical density of a culture growth solution.
44. The method of Claim 35, wherein said gene product is a polypeptide.
45. The method of Claim 35, wherein said gene product is an RNA.
46. The method of Claim 44, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.
47. A compound identified using the method of Claim 35.
48. A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242 or with activity against the product of said gene into a population of cells expressing a gene.
49. The method of Claim 48, wherein said compound is an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof.
50. The method of Claim 49, wherein said proliferation inhibiting portion of one of SEQ ID NOs. 405-485 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.
51. The method of Claim 48, wherein said compound is a triple helix oligonucleotide.
52. A preparation comprising an effective concentration of an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.
53. The preparation of Claim 52, wherein said proliferation-inhibiting portion of one of SEQ ID NOs. 405-485 comprises at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.
54. A method for inhibiting the expression of a gene in an operon required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid, said cell expressing a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242, wherein said antisense nucleic acid comprises at least a proliferation-inhibiting portion of said operon in an antisense orientation that is effective in inhibiting expression of said gene.



55. The method of Claim 54, wherein said antisense nucleic acid is complementary to a sequence of a gene comprising one or more of SEQ ID NOs.: 82-88, 90-242.

56. The method of Claim 54, wherein said antisense nucleic acid is a sequence of one of SEQ ID NOs.: 405-485, or a portion thereof.

57. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population.

58. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population.

59. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a sequence encoding said antisense nucleic acid into the chromosome of said cell into said cell population.

60. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population.

61. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide.

62. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell.

63. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by electroporation.

64. The method of Claim 54, wherein said antisense nucleic acid is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

65. The method of Claim 54 wherein said antisense nucleic acid is an oligonucleotide.

66. A method for identifying bacterial strains comprising the steps of:

providing a sample containing a bacterial species; and

identifying a bacterial species using a species specific probe having a sequence selected from the group consisting of SEQ ID NOs. 405-485, 82-88, 90-242.

67. A method for identifying a gene in a microorganism required for proliferation comprising:

(a) identifying an inhibitory nucleic acid which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with said inhibitory nucleic acid;

(c) determining whether said inhibitory nucleic acid from said first microorganism inhibits proliferation of said second microorganism; and

(d) identifying the gene in said second microorganism which is inhibited by said inhibitory nucleic acid.

68. A method for assaying a compound for the ability to inhibit proliferation of a microorganism comprising:

- (a) identifying a gene or gene product required for proliferation in a first microorganism;  
(b) identifying a homolog of said gene or gene product in a second microorganism;  
(c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;

(d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;

(e) contacting the sensitized microorganism of step (d) with a compound; and

(f) determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

69. The method of Claim 68, wherein said step of identifying a gene involved in proliferation in a first microorganism comprises:

introducing a nucleic acid comprising a random genomic fragment from said first microorganism operably linked to a promoter wherein said random genomic fragment is in the antisense orientation; and

comparing the proliferation of said first microorganism transcribing a first level of said random genomic fragment to the proliferation of said first microorganism transcribing a lower level of said random genomic fragment, wherein a difference in proliferation indicates that said random genomic fragment comprises a gene involved in proliferation.

70. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a database using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters.

71. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene.

72. The method of Claim 69, wherein the step of identifying a homolog of said gene in a second microorganism comprises expressing a nucleic acid which inhibits the proliferation of said first microorganism in said second microorganism.

73. The method of Claim 69, wherein said inhibitory nucleic acid is an antisense nucleic acid.

74. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of said homolog.

75. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding said homolog.

76. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises directly contacting said second microorganism with said nucleic acid.

77. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises expressing an antisense nucleic acid to said homolog in said second microorganism.

78. A compound identified using the method of Claim 68.

79. A method of assaying a compound for the ability to inhibit proliferation comprising:

- (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;
- (b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
- (c) contacting the proliferation-inhibited microorganism of step (b) with a compound; and
- (d) determining whether said compound inhibits proliferation of said sensitized second microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized second microorganism.

80. The method of Claim 79, wherein said inhibitory nucleic acid is an antisense nucleic acid which inhibits the proliferation of said first microorganism.

81. The method of Claim 79, wherein said inhibitory nucleic acid comprises a portion of an antisense nucleic acid which inhibits the proliferation of said first microorganism.

82. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense molecule against the entire coding region of the gene involved in proliferation of the first microorganism.

83. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding the gene involved in proliferation of the first microorganism.

84. A compound identified using the method of Claim 79.

85. A method for assaying compounds for activity against a biological pathway required for proliferation comprising:

sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;

contacting the sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

86. The method of Claim 85, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

87. The method of Claim 86, wherein said cell is an *E. coli* cell.

88. The method of Claim 85, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

89. The method of Claim 85, wherein said antisense nucleic acid is transcribed from an inducible promoter.

90. The method of Claim 89, further comprising contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sublethal level.

91. The method of Claim 90, wherein said sublethal level of said antisense nucleic acid inhibits proliferation by 8% or more.

92. The method of Claim 90, wherein said agent is isopropyl-1-thio- $\beta$ -D-galactoside (IPTG).

93. The method of Claim 91, wherein inhibition of proliferation is measured by monitoring the optical density of a liquid culture.

94. The method of Claim 85, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

95. A compound identified using the method of Claim 85.

96. A method for assaying a compound for the ability to inhibit cellular proliferation comprising:  
contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

contacting said cell with said compound; and  
determining whether said compound reduces proliferation to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

97. The method of Claim 96, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antisense nucleic acid to a gene or operon required for proliferation.

98. The method of Claim 96, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antibiotic.

99. The method of Claim 96, wherein said cell contains a temperature sensitive mutation which reduces the activity or level of said gene product required for proliferation of said cell.

100. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid encoding the same functional domain of said gene product required for proliferation of said cell to which said antisense nucleic acid is directed.

101. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid a different functional domain of said gene product required for proliferation of said cell than the functional domain to which said antisense nucleic acid is directed.

102. A compound identified using the method of Claim 96.

103. A method for identifying the pathway in which a proliferation-required nucleic acid or its gene product lies comprising:

expressing a sublethal level of an antisense nucleic acid directed against said proliferation-required nucleic acid in a cell;

contacting said cell with an antibiotic, wherein the biological pathway on which said antibiotic acts is known; and

determining whether said cell has a substantially greater sensitivity to said antibiotic than a cell which does not express said sublethal level of said antisense nucleic acid.

104. A method for determining the pathway on which a test compound acts comprising:

(a) expressing a sublethal level of an antisense nucleic acid directed against a proliferation-required nucleic acid in a cell, wherein the biological pathway in which said proliferation-required nucleic acid lies is known,

(b) contacting said cell with said test compound; and

(c) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

105. The method of Claim 104, further comprising:

(d) expressing a sublethal level of a second antisense nucleic acid directed against a second proliferation-required nucleic acid in said cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

(e) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid.

106. A purified or isolated nucleic acid consisting essentially of one of SEQ ID NOs: 358, 399-402.

107. A compound identified using the method of Claim 23.

108. A compound which interacts with the gene or gene product of a nucleic acid comprising a sequence of one of SEQ ID NOs: 82-88, 90-242 to inhibit proliferation.

109. A compound which interacts with a polypeptide comprising one of SEQ ID NOs. 243-357, 359-398 to inhibit proliferation.
110. A compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.

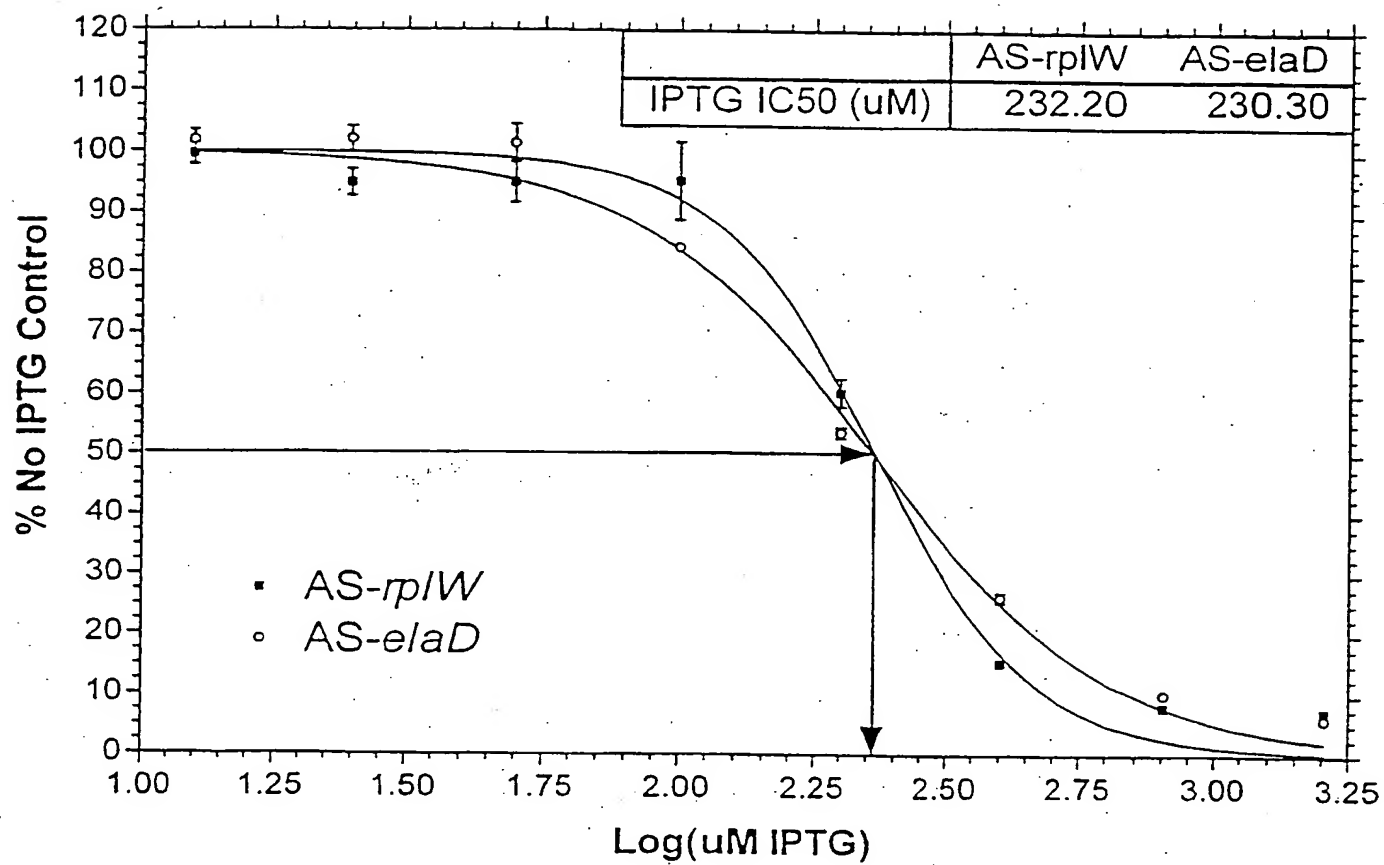
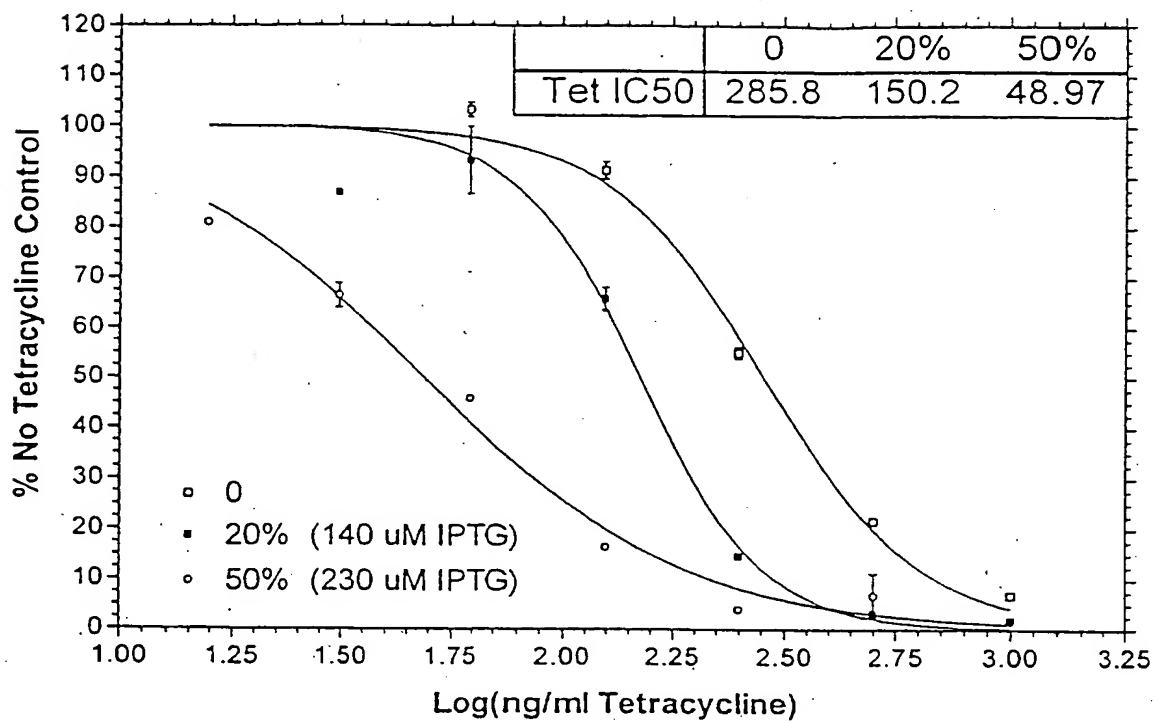
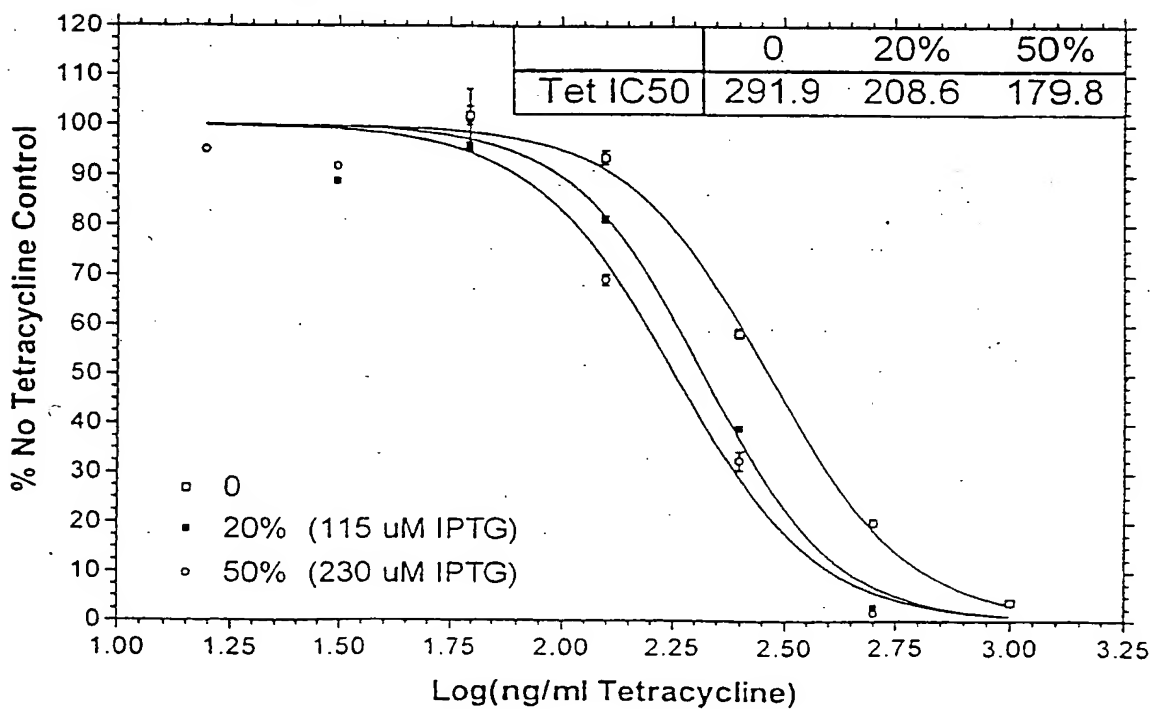


Fig. 1

**AS-rplW****Fig. 2a****AS-elaD****Fig. 2b**



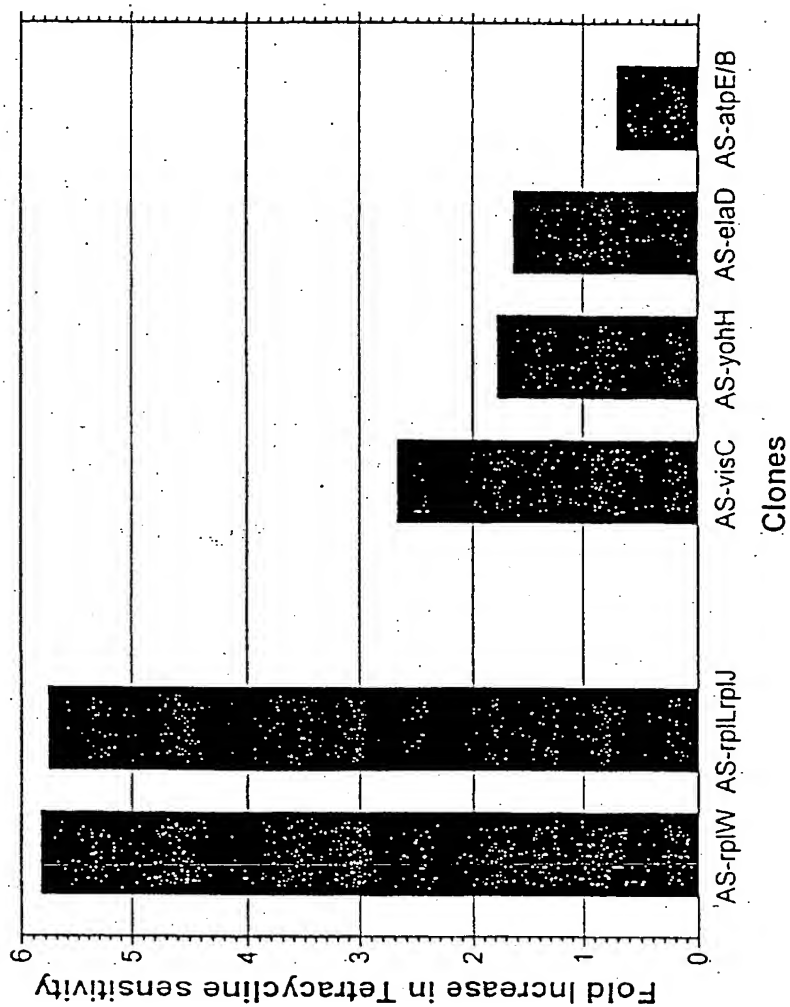


Fig. 3

## SEQUENCE LISTING

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Zyskind, Judith  
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 Trawick, John  
 Forsyth, R. Allyn  
 Froelich, Jamie M.  
 Carr, Grant J.  
 Yamamoto, Robert T.  
 Xu, H. Howard

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tctggacgca	gctgttgctg	gcaaaatcac	tgacgttgaa	gttctgaaag	cacagttcga	540
agaagaacgt	gttgcgctgg	tagcgaaaaa	tggtgaaaac	atcaacattc	gccgcgttgc	600
tgcgctggaa	ggcgacgttc	tgggttctta	tcagcacggt	gcgcgtatcg	gccgttctgg	660
ttgctgctaa	aagcgctgac	gaagaactgg	ttaaaccacat	cgttttgacc	ttgtgtgcaa	720
gccaaagccag	aattcagaga	aactttccgc	ttcaccggag	gtccccacca	cangganccc	780
cgattttntc	agcatgggtg	tcttcctncc	gagtt			815

<210> 6  
 <211> 403  
 <212> DNA

&lt;213&gt; E. Coli

&lt;400&gt; 6

caacactatt	ttgttgaccg	gaaaatggaa	cactttccgc	aatgcctggt	gctatcacgc	60
ttaaaccatt	tcattgcgat	ttacacagaa	cggacgtcct	gtcgcagtat	attaagtcgt	120
cgatagaaac	aagcattgaa	aggcacagca	gtagtcaaac	agtgtgaaac	gctactggcg	180
ccttacagcg	caaaaaggct	ggtgactaaa	aagtcaccag	ccatcagcct	gattttctcag	240
gctgcaaccg	gaagggttgg	cttattttaac	ttcaacttca	gcgccagctt	cttccagagc	300
ttttttcagt	gcttctgcgt	cgtctttgct	cacgccttct	ttcagagcag	ccggtgcaga	360
ttctaccagc	tccttagctt	ctttcagacc	caggccagtt	gcg		403

&lt;210&gt; 7

&lt;211&gt; 149

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 7

gagctttttt	cagtgtctct	gcgtcgtctt	tgctcacgcc	ttctttcaga	gcagccgggtg	60
cagattctac	caggtcttta	gcttctttca	gacccaggcc	agttgcgcca	cgtactgctt	120
tgataacagc	aactttgtta	gcgccagca				149

&lt;210&gt; 8

&lt;211&gt; 742

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(742)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 8

ccatctgtcc	attgagcgga	cagttttgtgc	aacactatatt	tggtgaccgg	aaaatggaac	60
actttccgca	atgcctgttg	ctatcacgct	taaaccattt	cattgcgatt	tacacagaac	120
ggacgtcctg	tcgcagtata	ttaagtcgtc	gatagaaaca	agcattgaaa	ggcacagcag	180
tagtcaaaca	gtgtgaaacg	ctactggcgc	cttacagcgc	aaaaaggctg	gtgactaaaa	240
agtcaccagc	catcagcctg	atcttctcagg	ctgcaaccgg	aagggttggc	ttattttaact	300
tcaacttcag	cgccagcttc	ttccagagct	tttttcagtg	cttctgcgtc	gtctttgtct	360
acgccttctt	tcagagcagc	cgggtgcagat	tctaccaggt	cttttagcttc	tttcagaccc	420
aggccagttg	cgccacgtac	tgctttgata	acagcaactt	tgtagcgcc	agcagctttc	480
agaattacgt	cgaattcagt	tntttcttca	gcagcttcaa	ccgggccagc	agctacagct	540
acagcagcag	caagcggaaa	caccgaattt	ttcttccatt	gcagagatca	gttctacaac	600
cgtccattac	agacatagct	gcaactgctt	caatgatatt	gatcttttagt	ggatagacat	660
ttaaattggt	cctgaattat	caagaaataa	gtnttatatc	taagccgaaa	tgcgttaaaa	720
aagataactg	ngattaaagc	ag				742

&lt;210&gt; 9

&lt;211&gt; 421

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 9

agtagtcaaa	cagtgtgaaa	cgctactggc	gccttacagc	gcaaaaaggc	tggtgactaa	60
aaagtcacca	gccatcagcc	tgattttctca	ggctgcaacc	ggaaggggtg	gcttatttaa	120
cttcaacttc	agcgccagct	tcttccagag	cttttttcag	tgcttctgcg	tcgtctttgc	180
tcacgccttc	tttcagagca	gccgggtgcag	attctaccag	gtcttttagct	tctttcagac	240
ccaggccagt	tgcgccacgt	actgctttga	taacagcaac	tttgtttagcg	ccagcagctt	300
tcagaattac	gtcgaattca	gttttttctt	cagcagcttc	aaccgggcca	gcagctacag	360
ctacagcagc	agcagcgga	acaccgaatt	tttcttccat	tgccagagatc	agttctacaa	420
c						421

<210> 10  
 <211> 126  
 <212> DNA  
 <213> E. Coli

<400> 10

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agagcctttt tcagtgccttc tgcgtcgtct ttgctcacgc cttctttcag agcagccggt    60
gcagattcta ccaggtcttt agcttctttc agaccacaggc cagttgcgcc acgtactgct    120
ttgata                                     126
```

<210> 11  
 <211> 262  
 <212> DNA  
 <213> E. Coli

<220>

<221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

<400> 11

```
ctgcaaccgg aagggttggc ttatttaact tcaacttcag cgccagcttc ttccagagct    60
tttttcagtg cttctgcgtc gtctttgctc acgccttctt tcagagcagc cgntgcagat    120
tctaccaggt ctttagcttc tttcagaccc aggccagttg cgccacgtac tgctttgata    180
acagcaactt tgttagcgcc agcagctttc agaattacgt cgaattcagt tttttcttca    240
gcagcttcaa ccgggcccagc ag                                     262
```

<210> 12  
 <211> 202  
 <212> DNA  
 <213> E. Coli

<220>

<221> misc\_feature  
 <222> (1)...(202)  
 <223> n = A,T,C or G

<400> 12

```
gcgcataccc tgcagcatcg gcccgatgga gatcagggtcg gcagaacgct gtaccgcttt    60
gtaggcgggtg ttaccgggtgn tcagatccgg gaagatgaac acggtagcgc gacctgcaac    120
cggagagttc ggcgcttttg attncgcaac gtcagccatt accgcagcgt cgtactgcag    180
cggaccggcg atcatcaggt ca                                     202
```

<210> 13  
 <211> 261  
 <212> DNA  
 <213> E. Coli

<400> 13

```
tctaggagta agaatagctt caaattcagc agttgacagt ggcataaacg taactggtga    60
cttttgcctg gcatgacgcc gggctttttt tattattccg tgacttccag cgtagtgaag    120
gcaaacttct cgccatcaaa tagcccttga ctggttagtt ttagcgcggt gatcactggc    180
agagaaagaa acgccatctg aataaacggc tcatcgggta acggaccgca ttcacggggc    240
gcggctttca aggcgtcaat t                                     261
```

<210> 14  
 <211> 224  
 <212> DNA  
 <213> E. Coli

<400> 14

ttcttttttt	cgtaacggt	gtccagaatc	attttattta	cctcggggta	cttatgctga	60
tttttattat	tatggggaag	gtgttattta	tgagtttcat	ttatgccgta	acgacaatga	120
actcgggaat	tagtataagc	agcgcgagaa	taataatcat	tgtgcaaag	ctaatttaaat	180
taatactatt	taaatattat	tttgagcata	tgacataag	gttg		224

<210> 15  
 <211> 232  
 <212> DNA  
 <213> E. Coli

<400> 15						
aattcccttc	tttttttcgt	caacgggtgtc	cagaatcatt	ttatttacct	cgggtactta	60
tgctgatttt	tattattatg	gggaagggtgt	tatttatgag	tttcatttat	gccgtaacga	120
caatgaactc	gggaattagt	ataagcagcg	cgagaataat	aatcattgtg	caaagtctaa	180
tttaattaat	actatttaaa	tattattttt	agcatatgca	cataagggtg	gg	232

<210> 16  
 <211> 212  
 <212> DNA  
 <213> E. Coli

<400> 16						
aatagcgggt	atgcacgcct	ttcttttttt	cgtaacggt	gtccagaatc	attttattta	60
cctcgggtac	ttatgctgat	ttttattatt	atggggaagg	tggtatttat	gagtttcat	120
tatgccgtaa	cgacaatgaa	ctcgggaatt	agtataagca	gcgcgagaat	aataatcatt	180
gtgcaaagtc	taatttaatt	aatactattt	aa			212

<210> 17  
 <211> 433  
 <212> DNA  
 <213> E. Coli

<400> 17						
ccttgtaaat	tatcgcccg	ggcataaaaa	ctgcgtccaa	acgccgtctt	tgccagcagc	60
caggccataa	atgccaccag	aattatcgtc	aaccaacca	ttgctgaaac	gccaagcagc	120
agcggggcgg	agagctgttt	cagttcggcg	ggtaaccctt	caatccattt	gccgccagtc	180
cacagcaaca	tgatgcctct	gtacaaccct	aacgtgccaa	gggtggcaac	aatggcaggg	240
atcttttagcc	acgcgaccag	gacaccgttg	aaaaatccc	cgagcaaacc	aagcagtaaa	300
gtcgcgacac	aagcaacagg	tagtgaatat	cctgcgttca	gtaacatccc	caacagcacc	360
gcgcacattc	cggtaatcga	acccactgaa	acatcaatat	tgccgcgtaag	cattaccagc	420
gtcgcgcccc	ttg					433

<210> 18  
 <211> 658  
 <212> DNA  
 <213> E. Coli

<400> 18						
cgtgcgcttc	cggttggtgc	aaccgcgcaa	atggcgcggc	ggtaagtatg	gcgggggttat	60
tccttccccg	ttgaggacac	cggttggtca	ggttgaccat	acgcttaagt	gacaaccccg	120
ctgcaacgcc	ctctgttatc	aattttctgg	tgacgtttgg	cggtatcagt	tttactccgt	180
gactgctctg	ccgccctttt	taaagtgaat	tttggtgatg	ggatgaatgcg	gctgagcgca	240
cgcggaacag	ttaaaaccaa	aaacagtgtt	atgggtggat	tctctgtatc	cggcggtta	300
tgtaactgg	ttaacgtcac	ctggaggcac	caggcactgc	atcacaaaa	tcattgttga	360
ggacgcgata	atgaaaacgt	tattacaaa	cgtaataacg	tctgaagggt	gttttgaaat	420
tggtgtcact	atcagtaacc	cagtatttac	tgaagatgcc	attaacaaga	gaaaacaaga	480
acgggagcta	ttaaataaaa	tatgcattgt	ttcaatgctg	gctcggtttac	gtctgatgcc	540
aaaaggatgt	gcacaatgaa	ttcagcattt	gtgcttggtc	tgacagtttt	tcttggttcc	600
ggagagccag	ttgatattgc	agtcaagtgg	tcacaggaca	atgcaggagt	gtatgact	658

<210> 19

<211> 588  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)... (588)  
 <223> n = A,T,C or G

<400> 19

gtgactgctc	tgccgccctt	tttaaagtga	atthttgtgat	gtggtgaatg	cggctgagcg	60
cacgcggaac	agttaaaacc	aaaaacagt	ttatgggtgg	attctctgta	tccggcggtta	120
attgttaact	ggttaacgtc	acctggaggc	accaggcact	gcatcacaaa	attcattggt	180
gaggacgcga	taatgaaaac	gttattacca	aacgttaata	cgtctgaagg	ttgttttgaa	240
attggtgtca	ctatcagtaa	cccagtatth	actgaagatg	ccattaacaa	gagaaaacaa	300
gaacgggagc	tattaaataa	aatatgcatt	gtttcaatgc	tggctcgttt	acgtctgatg	360
ccaaaaggat	gtgcacaatg	aattcagcat	ttgtgcttgt	tctgacagtt	tttcttggtt	420
ccggagagcc	agttgatatt	gcagtcagtg	ttcacaggac	aatgcangag	tgtatgactg	480
cagcaaccgc	aacagaaaat	tcccggtaac	tgttaccgcg	tcgataaagt	tattcaccag	540
gataatatcg	aaatcccggc	aggtctttaa	aacagttccg	taataaat		588

<210> 20  
 <211> 101  
 <212> DNA  
 <213> E. Coli

<400> 20

gatccagcaa	gaagatgcgg	ttgtaccgtc	atcacgcaga	tgcgcaaagc	tactcagcaa	60
ctgacctttc	ttcgcaataa	gcacgccatt	agcgtcatag	a		101

<210> 21  
 <211> 465  
 <212> DNA  
 <213> E. Coli

<400> 21

tcgcgtgttt	accttcaaca	tcggtaactt	tctggcggat	agtttcacgg	taagcaacct	60
gcggtttacc	tacgttcgct	tcaacgttga	attcacgctt	catacgggtc	acgatgatgt	120
cgaggtgcag	ttcgcccata	cccgcgatga	tggtctggtt	agattcttcg	tcagtccata	180
cacggaaaga	cgggtcttct	ttagccagac	ggcccagagc	cagacccatt	ttttcctggt	240
cagctttggt	tttcggttca	actgcgatgg	agattaccgg	ctcaggggaat	tccatacgtt	300
ccagaatgat	cggcgcaccc	gggtcacaca	gggtgtcacc	agtggttacg	tctttcagac	360
cgatagcagc	agcgaatgct	cccgcgcgaa	cttctttgat	ctcttcacgt	ttgttagcgt	420
gcatctgaac	gatacgaccg	aaacgctcac	gtgcagcttt	cacgg		465

<210> 22  
 <211> 859  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)... (859)  
 <223> n = A,T,C or G

<400> 22

tgatcggctc	aagcagaact	ggtttcgctt	tcttaaagcc	ttcttttaaag	gcgatagaag	60
cagccagttt	aaacgccagt	tcagaggagt	caacgtcatg	gtaagaaccg	aagtgcagac	120
gaatacccat	gtctactacc	gggtagcctg	ccagcggacc	tgctttcagc	tgttcctgga	180
tacctttatc	aacggccggg	atgtattcgc	cagggattac	accaccttta	atgtcgttga	240
tgaactcgta	gcctttcggg	tttgaaccgc	gctccagcgg	gtacatgtcg	ataacaacat	300

gaccatactg	accacgacca	ccagactggt	tgcggtggtt	accttcaaca	tcggttaactt	360
tctggcggat	agttttcacgg	taagcaacct	gcggtttacc	tacgttcgct	tcaacggtga	420
attcacgctt	catacgggtca	acgatgatgt	cgagggtgcag	ttcgcccata	cccgcgatga	480
tggctctggt	agattcttcg	tcagtcacata	cacggaaaga	cggtcttctt	ttagccagac	540
gggccanagc	cagacccatt	ttttcctggt	cagctttggt	tttcggtcaa	ctgcgatgga	600
gattaccggc	tcanggaatt	tccatacctt	ccaggaatga	tcggcgcatt	ccggtcaaac	660
anggngtacc	aggggggtac	ntntttttta	nancgattgc	cagcancgga	tntnncccg	720
gccnaacttc	tttggaacnn	tttaccggtt	ggtaaccngc	ctttttnaacn	atccaaccga	780
aaaagngtta	anngccantt	ttccnggngt	tnanntncgg	nttcccngaa	ntaaccncnc	840
cggggttnaac	ccngnaaaa					859

&lt;210&gt; 23

&lt;211&gt; 269

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 23

ctttcttaaa	gccttcttta	aaggcgatag	aagcagccag	tttaaaccgc	agttcagagg	60
agtcaacgtc	atggtaagaa	ccgaagtgc	gacgaatacc	catgtctact	accgggtagc	120
ctgccagcgg	acctgctttc	agctgttcct	ggataccttt	atcaacggcc	gggatgtatt	180
cgccagggat	tacaccacct	ttaatgtcgt	tgatgaactc	gtagcctttc	gggtttgaac	240
ccggctccag	cgggtacatg	tcgataaca				269

&lt;210&gt; 24

&lt;211&gt; 330

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 24

gttttgggga	gatgtaagg	ctaactctgaa	tggctgcatt	ccttggttta	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tggtttacag	120
ctgactcctt	tggtcttata	acacaaggaa	acgtacttaa	gggtgcgtccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaattg	catcaattaa	ataaatataa	tggcgttaag	gcttcccagt	300
aatataatta	atactctact	tccagagtag				330

&lt;210&gt; 25

&lt;211&gt; 471

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(471)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

gttttgggga	gatgtaagg	ctaactctgaa	tggctgcatt	ccttggttta	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tggtttacag	120
ctgactcctt	tggtcttata	acacaaggaa	acgtacttaa	gggtgcgtcc	gtgaaccag	180
tcggacgcac	ctttaataac	tataaataag	tgtctgggca	gatactatat	aaattaactt	240
agtgaatgat	tatgctaatt	tcattcaatta	aataaatata	atggcgttaa	ggcttcccag	300
tattataatt	aatactctac	ttccagagta	gaatattaaa	ttttatccgc	gtgggtgcac	360
agcacaaaatt	tatcccacaa	ctgttcttct	gtctcgacat	gccccccgat	ctttnacaaa	420
tantattggg	ggattnggcc	cncctttttg	ncagggttgg	gtcntctnat	g	471

&lt;210&gt; 26

&lt;211&gt; 379

&lt;212&gt; DNA

&lt;213&gt; E. Coli



<220>  
 <221> misc\_feature  
 <222> (1)...(379)  
 <223> n = A,T,C or G

<400> 26

natctgantg	gctgcattcc	ttgtttaagg	aaacccgaat	gactgattgc	cgataacctga	60
ttaaaccgggt	catcaaaatc	atcattgctg	ttttacagct	gacccctctg	ttctttataac	120
acaaggaaac	gtactttaagg	tgcgtccggt	gaaccagtcg	gacgcacctt	taataactat	180
aaataagtgt	ctgggcagat	actatataaa	tttaacttagt	gaatgattat	gctaattgtca	240
tcaattaaat	aaatataatg	gcgttaaggc	ttcccagtaa	tataattaat	actctacttc	300
cagagtagaa	tattaaattt	tatccgcgtg	gtgcatcagc	acaaatttat	cccacaactg	360
ttcttctgtc	tcgacatgc					379

<210> 27  
 <211> 799  
 <212> DNA  
 <213> E. Coli

<400> 27

aaagatgatg	tgatgagaaa	gtcaatttga	ataagacaat	attaagagct	aaaaaaatgt	60
caaaaaacac	taaatcaaaa	aataatggca	ttagaaaata	taatgcgaaa	acggaggtga	120
aattagttta	tttcaaatga	ggaaaaatctc	ccggcgaaaa	aaccggggaga	tgaaagtgtg	180
atgggtatca	aataaacaac	agaggagaaa	tttttaacgc	agccattcag	gcaaatcggt	240
taatcccat	gcctggcgga	taagttagcg	cttaacgcc	ggaagcgtgt	cggccagttt	300
caaaccaata	tcacgcagca	gttttttcgc	cggattggta	ccggaaaaaca	gatcgcggaa	360
tccctgcata	ccagccagca	tcaacgccgc	actgtgcttg	cggctacgct	catagcgacg	420
cagataaatg	tactgcccga	tgtctgggat	ccgtcgacct	gcagccaagc	ttgggctttt	480
cagcctgata	cagattaaat	cagaacgcag	aagcggctctg	ataaaacaga	atttgcctgg	540
cggcagtagc	gcggtgggtcc	cacctgaccc	catgccgaac	tcagaagtga	aacgcccgta	600
gcgcccgatg	gtagtgtggg	gtctcccat	gcgagagtag	ggaactgcc	ggcatcaaat	660
aaaacgaaag	gctcagtcga	aagactgggc	ctttcggttt	atctggtggt	tgtcggtgaa	720
cgctctctga	gtaggacaaa	tccgccggga	gcggattttg	aacgttgcca	aacaaccggc	780
ccggaaaagg	gtgggggct					799

<210> 28  
 <211> 636  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(636)  
 <223> n = A,T,C or G

<400> 28

aggggggtttg	ttgtgggcaa	tgatgcattt	aagttatcgt	ctgcagatag	aggagatatt	60
acaataaaca	acgaatcagg	gcatttgata	gtcaataccg	caattctatc	aggagatata	120
gtcactctaa	gaggaggaga	aattagggtg	gtattatagc	ttgtgcgcgc	catgattggc	180
gcgcaattta	aacttagtgc	tttacatcgc	tattgtcttg	atttctttga	attattttat	240
aaattaaaaa	aacgactgtt	atgtataagc	aaaggtcgaa	cgaaaaatac	attccaaata	300
aatgcttgct	taaatctcta	tatccttccc	cgaaaaatga	cacataaaaat	tgagatattc	360
caaaaagaga	tactacaaat	aaagatgcct	ttattttatt	attttotaata	aaaatagaag	420
caataaaaaa	taataacaat	gatataaatc	taatgttttt	aaatatattg	tcttttatgt	480
tagtaaatag	cgttagtagt	tttgattctc	catatattac	gtgtagtttt	ttatatacat	540
ggaaataatt	ntctttatac	tgagacatca	caccatcatc	aaatggaagt	ttgaagatgg	600
tgcttggttt	gctaaccaat	aaaaagagtg	cattcgc			636

<210> 29  
 <211> 757  
 <212> DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(757)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 29

cagcgggtcgt	atttttagca	tgggttttta	ttggcggcta	tgctgccccg	ggagcataaa	60
gatgaaaaaa	acaacgatta	ttatgatggg	tgtggcgatt	attgtcgtac	tcggcactga	120
gctgggatgg	tggtaacgtc	acctctaaaa	aatagcaaag	gctgcctgtg	tgcagccttt	180
gtgcaattta	agcggttaact	tttaatcttc	ctgtagataa	atagcacgac	aatcgcacca	240
ataacggcaa	ccacgaagct	gccaaaattg	aagccatcga	ctttaccaaa	gccaaacagc	300
gtgctgatcc	atccgccgac	tacggcaccg	actatcccca	gcaggatagt	cataaagaat	360
ccacctccat	ctttacctgg	catgatccac	ttcgccagaa	taccggcaat	aagcccaaaa	420
ataatccatg	acagaatgcc	cattgtttcc	tcacttatct	gttttgcat	agcgggttag	480
tcgctgataa	aaagcatagc	acaacatcgg	gagggcaaga	tttgtgacga	gcatcacgga	540
ggtttttttt	gcgatggcgc	agaaattgcg	ccatcaacga	tcagtgataa	ttaccaacca	600
caaacatcat	gttcgttttc	cgtgtcataa	gaaccgtacg	ggattcacca	gatcttttat	660
cacttcaagc	cggcacttct	ggcaccagca	aagtcatcgg	cgtctctggt	tcataatcga	720
ccggaaacgc	cattgctggt	attggtgaen	gtcacgg			757

&lt;210&gt; 30

&lt;211&gt; 392

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 30

aattacagaa	aaaggaggca	atatcgggta	aaggcattag	cccagcgaat	acgtcgggct	60
acaaatatta	ttgtgctgca	ggtgttttag	cgggttggtg	atccacaggt	tctaactgga	120
agaccacatc	gacctgatca	tcaaactgaa	tagcggcctg	ctcgtaagtt	tcctgggcgg	180
acaccggcgc	ggcatcggtc	ttcatcatcc	gcaccattgg	gctgggctga	tagttggaaa	240
catggttagc	cacgctatat	accggcccca	gtttacgatg	aaagccgttc	gccagttcct	300
gcgcctgatg	aatcgcggtt	tcaatcgctg	ccttacgcgc	tttgtcttta	taggcatccg	360
gctgcgccac	gcccagcgac	acagaacgaa	tt			392

&lt;210&gt; 31

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 31

ctatccttga	tgaaccgcgc	agcaaagata	ggtgattacg	tcattggtttt	acagaaaatt	60
acagaaaaag	gaggcaatat	cgggttaaagg	cattagcccc	acgaatacgt	cgggctacaa	120
atattattgt	gctgcaggtg	ttttagcggg	ttgttgatcc	acaggttcta	actggaagac	180
cacatcgacc	tgatcatcaa	actgaatagc	ggcctgctcg	taagtttcct	gggcggacac	240
cggcgcggca	tcggctttca	tcatccgcac	cattgggctg	ggctgatagt	tggaaacatg	300
gtagcgcacg	ctatataaccg	gccccagttt	acgatgaaa	ccgttcgcca	g	351

&lt;210&gt; 32

&lt;211&gt; 762

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(762)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 32

aattatgaaa	cactgtctgg	aatcgtctga	atgacgggca	catttgcgag	cacgcatcca	60
------------	------------	------------	------------	------------	------------	----

gtaataacac	aggaaactat	tttatctacg	cgttagcgat	agactgcttg	catggcgaaa	120
ggaggtaagc	cgacgatttc	agcgggacgc	tgaaacggga	aagccctcc	cgaggaagg	180
gccataaata	aggaaaggt	catgatgaag	ctactcatca	tcgtggtgct	cttagtcata	240
agcttccccg	cttactaaga	ctaccagggc	gggggaaacc	ccgctctacc	ctcaactctg	300
aaagtatgcc	ttcacgataa	gattgtcaat	ccgcaggctt	tgtagtctgc	gaccttgcca	360
gcaaatattc	tttgcgagtc	gttacgcaat	aatcacagag	gaaactat	tattcacgcg	420
ttagcgatag	actgcattca	gggcgaaagg	aggtaagccg	atgatttcag	cgggacgctg	480
aaacgggaaa	gcctctcccc	gagaagagg	cttttaataa	ggaaagggtt	atgatgaagc	540
acgtcatcat	actgggtgata	ctcttagtga	ttagcttcca	ggcttactaa	gaacaccagg	600
gggaggggga	aacctcttcc	taacctcac	ttctgaaatt	gggtgctatg	acgctggcgt	660
tactgcttan	cgctaccagt	ttgtctgccc	tggcggttgt	aacgccagat	cggtaccgct	720
ttggatattt	taatgaaagc	cgacaaatca	atcancgtga	cg		762

<210> 33  
 <211> 293  
 <212> DNA  
 <213> E. Coli

gcacatttgc	gagcacgcat	ccagtaataa	cacaggaaac	tattttatct	acgcgttagc	60
gatagactgc	ttgcatggcg	aaaggaggta	agccgacgat	ttcagcgga	cgctgaaacg	120
ggaaagcccc	tcccaggagaa	ggggccataa	ataaggaaag	ggtcatgatg	aagctactca	180
tcatcgtggt	gctcttagtc	ataagcttcc	ccgcttacta	agactaccag	ggcgggggaa	240
accccgctct	accctcactc	ctgaaagtat	gccttcacga	taagattgtc	aat	293

<210> 34  
 <211> 633  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(633)  
 <223> n = A,T,C or G

atttacactt	tttacgaaat	catgggatca	ctaacaaaat	atcgcttgct	agttatattg	60
tatggcagga	aagatatgcg	actgatatta	cagatcccca	aagtggagag	tttatgacca	120
ttaaaaaata	gatgttgctg	ggtgcgcttt	tgctgggttac	cagtgccgcc	tgggccgcac	180
cagccaccgc	gggttcgacc	aatacctcgg	gaatttctaa	gtatgagtta	agtagtttca	240
ttgctgactt	taagcatttc	aaaccagggg	acaccgtacc	agaaatgtac	cgtaccgatg	300
agtacaacat	taagcagtgg	cagttgcgta	acctgcccgc	gcctgatgcc	gggacgcact	360
ggacctatat	gggtggcgcg	tacgtgttga	tcagcgacac	cgacggtaaa	atcattaaag	420
cctacgacgg	tgagattttt	tatcatcgct	aaaaaaagcc	ccctcatcat	gagggggaaa	480
tgcagacacc	ttgntatttt	ttattattag	ccacttgctc	gtcttgcttg	gtattaagtc	540
gtatttcacg	ttgattaatg	cnggtggctc	cagtgcgcc	gattaacttt	gtttggatcg	600
aagacgtagt	aactggctgg	ttatcggaat	tgg			633

<210> 35  
 <211> 569  
 <212> DNA  
 <213> E. Coli

tatggcagga	aagatatgcg	actgatatta	cagatcccca	aagtggagag	tttatgacca	60
ttaaaaaata	gatgttgctg	ggtgcgcttt	tgctgggttac	cagtgccgcc	tgggccgcac	120
cagccaccgc	gggttcgacc	aatacctcgg	gaatttctaa	gtatgagtta	agtagtttca	180
ttgctgactt	taagcatttc	aaaccagggg	acaccgtacc	agaaatgtac	cgtaccgatg	240
agtacaacat	taagcagtgg	cagttgcgta	acctgcccgc	gcctgatgcc	gggacgcact	300
ggacctatat	gggtggcgcg	tacgtgttga	tcagcgacac	cgacggtaaa	atcattaaag	360
cctacgacgg	tgagattttt	tatcatcgct	aaaaaaagcc	ccctcatcat	gagggggaaa	420

tgcagacacc	tigtattttt	ttattattag	ccacttgctc	gtcttgcttg	ttattagtcg	480
tatttcacgt	tgattaatgc	ggttgcctcc	agtgcgccag	atttaacttt	gtttgtatcg	540
tagacgtagt	aactggctgg	tatcggaat				569

<210> 36  
 <211> 338  
 <212> DNA  
 <213> E. Coli

<400> 36						
cgtattcaca	tcctttttgat	tggtgataac	atgcgaatcg	gtattatttt	tcgggttgta	60
atcttcatta	cagcggtcgt	atttttagca	tggtttttta	ttggcggcta	tgctgccccg	120
ggagcataaa	gatgaaaaaa	acaacgatta	ttatgatggg	tgtggcgatt	attgtcgtac	180
tcggcactgc	ctgggatggg	ggtaacgtca	cctctaaaaa	atagcaaagg	ctgcctgtgt	240
gcagcctttg	tgcaatttaa	gcgttaactt	ttaatcttcc	tgtagataaa	tagcacgaca	300
atcgaccaa	taacggcaac	cacgaagctg	cctaaatt			338

<210> 37  
 <211> 375  
 <212> DNA  
 <213> E. Coli

<400> 37						
ctgaatattt	aaaaaggaaa	acgacatgaa	accgaagcac	agaatcaaca	ttctccaatc	60
ataaaatatt	tcctgtggagc	attttattat	tgaatataga	ggtttaactc	cggtaaaaaa	120
caaagaagca	ttgaatgcag	ggaaaaataa	tatggccata	aaaaacatcg	aaagaaactc	180
ttttaattta	acatgtaaac	gcatgggtta	tcctcatatc	acgggtggag	tgtaagaac	240
atacataaat	ggagtcattg	tttccctttt	ccatttatca	agttcctgtt	gccgttttag	300
tccatctcta	attgcatatt	ttaatttttc	tgataaatgg	cattgagcat	cgatttcatt	360
taaaacaact	gtaca					375

<210> 38  
 <211> 446  
 <212> DNA  
 <213> E. Coli

<400> 38						
ttacgatagc	tattagtaaa	aatataagag	ttagctgtat	tgttatgtct	gtggcgaaat	60
tgactacctt	cggttttttg	attaagaatg	attttattat	cgtaagtaaa	attacatgaa	120
tattttaaaaa	ggaaaacgac	atgaaaaccga	agcacagaat	caacattctc	caatcataaa	180
atatttccgt	ggagcatttt	attattgaat	atagaggttt	aactccggta	aaaaacaaag	240
aagcattgaa	tgacgggaaa	aataatatgg	ccataaaaaa	catcgaaaga	aactctttta	300
atttaacatg	taaacgcag	gttaatcttc	atcacaggg	tggagtgtta	agaacataca	360
taaatggagt	catgttttcc	cttttccatt	tatcaagttc	ctgttgccgt	tttagtccat	420
ctctaattgc	atattttta	ttttct				446

<210> 39  
 <211> 392  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(392)  
 <223> n = A, T, C or G

<400> 39						
tcaccccggt	gccgattttc	aggcatcctg	atttaactta	gcacccgcaa	cttaactaca	60
ggaaaaacaaa	gagataaatg	tctaactctg	atgcaaactg	agccgatttt	ttaatcttta	120
cggactttta	cccgcctggg	ttattaattg	cactgtgnatc	cgggcggttcg	cccgccttta	180
tcacaatagg	ctgtgtagcc	tgggcctgtt	tctctttcac	ccgcgccaga	gcggcagcaa	240

tcgcacatctt atctttggct gcaggttgaa cggctgcgct cttatgtcgt tcaaggcgag	300
ccgctttttc gcgctccaga cgagcctggc gcgcttcgaa acgcgctttg gcttctgcgg	360
cncgcttttc ttcctgacga atagccgcaa tt	392

&lt;210&gt; 40

&lt;211&gt; 208

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 40

taataacgct atctgaggat aaagcagaat aggtggttaa cccagacat aaaccgagga	60
aaataatggt attgtatttc ataatctatt gtcccttagc gacagattgc tgtctgctgg	120
ttcagtaagg taccaggaga aacttcagga agcttgtagt cgacaataca gtttgagttt	180
ttatctttgc cccatgaaac ctgtaatt	208

&lt;210&gt; 41

&lt;211&gt; 342

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 41

catcctcaat accgttaaat gcaacccgaa cccccgttgt ccccttgctg cattcactta	60
acgtaatctg aaaagggacg gctggacttg tgctaccggt cgttggaaat tgtctggcac	120
tgtttttttg gagatctacg gtaaaattaa gcgaatccga tgagactgtg cagccataat	180
cgaggacgcg cccgctaatt ttaataacgc tatctgcgga taaagcagaa taggtggtta	240
accccagaca taaaccgagg aaaataatgt tattgtattt cataatctat tgctccctag	300
cgacagattg ctgtctgctg gttcagtaag gtaccaggag aa	342

&lt;210&gt; 42

&lt;211&gt; 841

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(841)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 42

agatttactg ccaatttccg gcagatcgga aagggttaaa ccatattgat ccataagggt	60
acgaatcacg gctataccgc caggcatggc ttgagccatg gcattaaatt ccgcaaattc	120
gggcgctgat tcttcccacg cggttatttt ggacacacacc agatccagca aggggtnttc	180
aggatcggtg agcagcagat gatctaccag ttncagcgcc tgggtgtatt gntccttggt	240
ctgaataccc gnnagaaaag gtgccacagc anttagcttn tctcctgctt gcaagatgtc	300
tggcaatngc aatcattttt tgcaattant acgatgnaca ncngtaaaaga aatcgnattt	360
ttntatgccg tcataacttt acgtatgtan cactttttgc nattcnaaaa aagaccattn	420
gctncaacac gtaaattna ttgncccccna catttanaac ataaatgntt aaaattttcc	480
ccccnccnna ttttaagntn ttanagaat ngggaattac ctgcttttna atgnactcan	540
antttttng naataattcc tntatcnaa ctntttttcn cccaanagnc nnccaaattn	600
cggtttntn nttnnchnng cnttttttta cccnanaann tttattcaan nccctttttg	660
tagnctattt naagnggnet ttnttnnatt aactttccnn ttggncaaat tttggcnnat	720
ttttatatan aattntctta tntcntaatt tnggnanccc cngatgnaan tttatggngg	780
gantcccnnt cccnttttaa tnnatgntct gggntatttt taaancctnn attaanann	840
c	841

&lt;210&gt; 43

&lt;211&gt; 215

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 43

aataacrtttt	cgttaggcag	ttttgggtgt	gagttgcaag	aggggagact	actgaataac	60
tcaagtttta	taatcgaggg	gaaaatgggt	atggcgttca	tagcaaaacg	ccctcaacca	120
taaaggtcga	gggcgcttaa	gatgttaaaa	acccgctatc	cgttaaaaaa	caatgttcaa	180
ctaaggtcag	tgacattgcg	ctaaaaaagc	gaatt			215

<210> 44  
 <211> 395  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(395)  
 <223> n = A,T,C or G

<400> 44						
gcattattca	tgagaaatgt	gtatcgtaaa	tcaactgaaa	ttaacgcaac	catttggttat	60
ttaaggttta	attatctgtg	tgtgatattt	tattgaatgt	tttaaattatt	gtttttattg	120
gcattgctat	aatattgggt	atcatttgct	gaatggattc	agtcttaatg	agtgggtttt	180
taagggacag	gcataagagta	atgatacgta	tgcataacca	acatctttac	tcattatgtc	240
attgaatgtt	gaccctatgt	gtttatgaag	gagaggtatt	ttcagttgat	ctggattgnt	300
aaattcatat	aatgcgcctt	tgctcatgaa	tggaatgccag	tatgtagtgg	gaaattataa	360
atattgaaat	agtccaacta	cttcttttatt	accaa			395

<210> 45  
 <211> 883  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(883)  
 <223> n = A,T,C or G

<400> 45						
ataatcaggt	aagaaaaggt	gcgcgggagat	taccgtgtgt	tgcgatatat	tttttagttt	60
cgcggtggcaa	tacatcagtg	gcaataaaaac	gacatatcca	gaaaaatata	cactaagtga	120
atgatatctt	ccgattttatc	ttaatcgttt	atggataacg	gcaaagggct	tcgttttttc	180
ctatacttat	tcagcactca	caaataaaagg	aacgccaatg	aaaattatac	tctgggctgt	240
attgattatt	ttcctgattg	ggctactggg	ggtgactggc	gtatttaaga	tgatatttta	300
aaattaatta	atgtcatcag	gtccgaaaaat	aacgagaata	tttcagtctc	tcctcctggt	360
gcgctcctgt	catgtgcatt	gcttcatata	atcactggcg	caaggagcgc	cgcaggcgna	420
gnntgcncgn	cgncccacct	naccccatgc	cgaacttcag	aantgaaaac	nccntaacnc	480
cgatngtcgg	cgggngcctc	cccatgcnan	agtangggaa	ntgccangcg	ncnnattaaa	540
cgaaaggctn	attncaaaga	ctgggccttn	cntttatctg	atgtttgtcg	gagaacgctc	600
tcctgagnan	gacaaatncc	gccgggagcg	gatttgaacn	ttgcgaagca	accgncccna	660
agggngnngt	cntgacnccc	nnctctanct	nnngccttc	ttttgcttna	angnccctct	720
ancngatggc	ctttttngcc	ntctacccaa	cnntttgggt	aatgcttnta	aaancctttc	780
cannntncaa	tcngtntn	cccattccnn	tnntgaaagn	ntnccntnccn	tgtncantnt	840
anntnnnggg	gnngngngcc	ggcggncccc	cccccccccc	ccc		883

<210> 46  
 <211> 1024  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(1024)  
 <223> n = A,T,C or G

&lt;400&gt; 46

gtttatggat	aacggcaaag	ggcttcggtt	tttccctatac	ttatttcagca	ctcacaaata	60
aaggaacgcc	aatgaaaatt	atactctggg	ctgtattgat	tattttcctg	attgggctac	120
tggtggtgac	tggcgtat	aagatgat	tttaaaatta	attaatgtca	tcagggtccga	180
aaataacgag	aatatttcag	tctctcatcc	tggtgcgctc	ctgtcatgtg	cattgcttca	240
tataatcact	ggcgcaagga	gcgcgcagag	tnctccnant	nnnnntnntt	ntntnnctnn	300
nccttcacna	tncnncncn	nantnnatag	nncaccnntn	ttntntcnntn	gnccnccctcc	360
nnncnnnnnn	ncatnnnate	ccactnnntt	tnctccannn	nnncnnnnntn	cannccnataa	420
antnncnacc	anntnacett	atacnnannc	nancnnnnnn	nnccactctn	nctcgnnctc	480
cccnttcnac	nnccannnnn	cancnntcnn	ctnnnnccct	nnntaattn	ttctnnctan	540
ntcctanccn	cnnacnnncc	cancnatccn	nnnatacant	cnattntntn	cnntcncntn	600
cnccnnttcc	nnctnnnncn	tnccnecatc	ccnnnannan	canntncccc	ncctnccctna	660
ccnccnccnc	ccnccatccc	nnccnncnt	ccnnantnga	caannnnaat	cncnnnnncn	720
nnnnnnnnnn	tnnnncnccn	gcncnncnt	nccptcacnc	tnnnnnncta	nanhnnntac	780
nntnaccnnt	cctnnacacn	tnccctnnng	antccnacna	ntnnnnnnanc	nanaacnctn	840
tnnnnccata	atcccacacc	acnccentnc	ancntntntt	ncntntcccc	ttcntatcnc	900
agctnnnnnt	nctntnnnnn	tnccnccenn	cnnactnchn	nnaccnncnn	cccantcagt	960
ccaccntccn	cnnccnnntn	nnncnancan	ctnnacacnc	cnantaacct	nntnncacct	1020
tccc						1024

&lt;210&gt; 47

&lt;211&gt; 236

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 47

atatacacta	agtgaatgat	atcttccgat	ttatcttaat	cggtttatgga	taacggcaaa	60
gggcttcggt	ttttccctata	cttatttcagc	actcacaaat	aaaggaacgc	caatgaaaat	120
tatactctgg	gctgtattga	ttattttcct	gattgggcta	ctgggtggtga	ctggcggtatt	180
taagatgata	ttttaaaatt	aattaatgtc	atcagggtccg	aaaataacga	gaatat	236

&lt;210&gt; 48

&lt;211&gt; 418

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(418)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 48

cggagattac	cgtgtgttgc	gatatatattt	ttagtttcgc	gtggcaatac	atcagtggca	60
ataaaacgac	atatccagaa	aaatatacac	taagtgaatg	atatcttccg	attnatctta	120
ntcgtttatg	gataacggca	aagggttcg	ttttttccta	tacttattca	gcactcacaa	180
ataaaggaac	gccaatgaaa	attatactct	gggctgtatt	gattattttc	ctgattgggc	240
tactggtggt	gactggcgta	tttaagatga	tattttaaaa	tttaattaatg	tcacaggtc	300
cgaaaataac	gagaatattt	cagtctctca	tcctgttgcg	ctcctgtcat	gtgcattgct	360
tcataataac	actggcgcaa	ggagcgcgca	nggggcggcc	aatcgccgcc	ggccccctg	418

&lt;210&gt; 49

&lt;211&gt; 550

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 49

ctgctagtta	cagggaacac	taatgacaga	cagctaaaag	ccctgtttta	ttacgtatta	60
caaacagggg	atgccagcg	tttctgtgca	tttattgggtg	agatagcgga	acgcgcacca	120
caagaaaagg	agaaactgat	gaccattgct	gacagattac	gtgaagaagg	cgcaatgcag	180
ggcaaacacg	aagaagccct	gcgtattgct	caggagatgc	tggaatagagg	tttagacaga	240
gagttagtta	tgatggtgac	ccgactttca	ccagacgatc	ttatcgcgca	aagccactaa	300

tcctgtaaca	ccgggagtta	actggcggat	gtttgctgta	aaccacatca	gcgaacgaca	360
tccgccagcg	cctcttctaa	atcgtaccag	cgaaacgcaa	aaccgccttc	ttccagccgt	420
ttaggcagcg	cgcggtgtcc	acctaatacc	agtactgaag	attcgcccat	taacagtcga	480
atggcggtcg	cggggacgcg	caaaatggcc	gggcgatgca	gcgcatgacc	gagcgcatgg	540
gcaaattggt						550

<210> 50  
 <211> 99  
 <212> DNA  
 <213> E. Coli

<400> 50	
ttggcatctc	ggtgttgccg
atcttcatga	tatccagccc
gccggaaaact	tcttcccaaa
cggttttgct	ggtatccatt
gagtcacgga	actgccct
	60
	99

<210> 51  
 <211> 259  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(259)  
 <223> n = A,T,C or G

<400> 51	
ccgtgccgag	atgatcctgt
naccatcatc	cgttgtgaag
tagtgattca	cgacttcaag
gcgcttttca	aaaggggtatt
ttggctttga	catattaggg
gctattccat	ttcatcgnc
aacaaaatgg	gtgcagtaca
tactcnttgg	aaatcaacac
aggaggctgg	gaatgccgca
gaaatataga	ttactttctt
taatagtgat	ntgtttcacg
cttttatttt	tnaanaaagt
tnggcttact	tcccggggn
	60
	120
	180
	240
	259

<210> 52  
 <211> 877  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(877)  
 <223> n = A,T,C or G

<400> 52	
cagcagagcg	cgcccttctt
cgtcagattt	cgcagtagtg
gtaatggtaa	tatccaaacc
acgaacgcgg	tcgactttat
cgtagtcgat	ttctgggaag
atgatctgct	cacggacacc
catgctgtag	ttaccacgac
cgtcgaaaga	cttagcggac
aggccacgga	agtcacggat
acgaggtaca	gcaatagtga
tcaggcgctc	aaagaactcc
cacatgcgtt	cgccacgcag
agttacttta	cagccgatcg
gatagccctg	acggattttg
aagcctgcaa	cagatttgcg
tgttttggtg	atcagcgggt
tttgaccgga	gattgctgcc
aggtctgctg	ctgcgttatc
cagcagtttt	ttgtcagcga
tcgcttcacc	aacacccatg
ttcagggtga	tcttctcgac
ccgagggact	tgcattgacag
aattgtagtt	aaactcagtc
atgagttttt	taactacttc
gtctttgtag	taatcatgca
gtttcgccat	cgtactactc
catgtcgggtg	aacgctctcc
tgagtaggac	aaatccgccg
ggagcggatt	tgaacgttgc
gaagcaacgg	cccggagggt
ggcgggcagg	acgcccgcga
taaaactgcc	ggcatcaaat
taagcagaag	gccatcctga
cggatggcct	ttttgcgttt
ctacaaaactc	ttttggttat
ttttctaaat	cattcaaata
tgtatccgnt	catcccatac
tatcgtatgat	aagctgtcaa
acatgagaat	ttaatcaatc
ttaaagtttta	ctgngttaaa
cttgggctgg	cagnttncca
atggcttaat	cagtnagagg
ccctatntta	acgaactngg
ctantttngg	tcaatcn
	60
	120
	180
	240
	300
	360
	420
	480
	540
	600
	660
	720
	780
	840
	877

<210> 53  
 <211> 291



<212> DNA  
<213> E. Coli

<400> 53

tgaacagcag	agatacggcc	agtgcggcca	atgttttttg	tcctttaaac	ataacagagt	60
cctttaagga	tatagaatag	gggtatagct	acgccagaat	atcgtatttg	attattgcta	120
gtttttagtt	ttgcttaaaa	atattgttag	ttttattaaa	tgcaaaacta	aattattggt	180
atcatgaatt	tgttgatga	tgaataaaat	ataggggggt	atagatagac	gtcattttca	240
tagggttata	aatgcgacta	ccatgaagtt	tttaattgaa	agtattgggt	t	291

<210> 54  
<211> 282  
<212> DNA  
<213> E. Coli

<400> 54

ttattaaatg	caaaactaaa	ttattggtat	catgaatttg	ttgtatgatg	aataaaatat	60
agggggggtat	agatagacgt	cattttcata	gggttataaa	tgcgactacc	atgaagtttt	120
taattgaaaag	tattgggttg	ctgataattt	gagctgttct	attcttttta	aatatctata	180
taggtctgtt	aatggatttt	atttttacaa	ttttttgtgt	ttaggcatat	aaaaatcaac	240
ccgccatatg	aacggcggtt	taaaatattt	acaacttagc	aa		282

<210> 55  
<211> 293  
<212> DNA  
<213> E. Coli

<220>

<221> misc\_feature

<222> (1)...(293)

<223> n = A,T,C or G

<400> 55

cggggtccgg	cgctcatcaa	caatcggggg	gcagcaaggg	gctgaaacgg	gaaagcccoct	60
cccgaagaag	gggccttgta	taaggaaagg	gttatgatga	agctcgtcat	catactgggt	120
gtgtngttac	tgttaagttt	cccgaacttac	taacaactca	tcagaggggg	gagaaatcoct	180
cccttaccct	tgttccttta	ctctaggttg	aaaaaacaac	agcgtcaata	ggcctgccat	240
gtacgaagcg	agatctgtga	accgctttcc	ggttagcctt	ttttatcctg	ttg	293

<210> 56  
<211> 300  
<212> DNA  
<213> E. Coli

<400> 56

tctgcgttcc	gctaaaagg	gcaaagtctc	aggacgttgc	agcgttttgc	gtgaccgctc	60
ggggaaggca	aaattgcctc	tgggaaagca	ttgcgcgggg	tccggcgctc	atcaacaatc	120
ggggggcagc	aaggggctga	aacgggaaag	cccccccgga	agaagggggc	ttgtataagg	180
aaagggttat	gatgaagctc	gtcatcatac	tggttggtgt	gttactgtta	agtttcccga	240
cttactaaca	actcatcaga	ggggggagaa	atcctccctt	acccttggtc	ctttactcta	300

<210> 57  
<211> 359  
<212> DNA  
<213> E. Coli

<400> 57

caacacagga	ggctgggaat	gccgcagaaa	tatagattac	tttctttaat	agtgatttgt	60
ttcacgcttt	tattttttcac	ctggatgata	agagattcac	tgtgtgaatt	gcatattaaa	120
caggagagtt	atgagctggc	ggcgttttta	gcctgcaaat	tgaaagagta	agagtcttcg	180
gcgggaaatt	attccccgct	tacttacggc	gttgcgcat	ctcattgcac	ccaaatttat	240

tcttcacaaa aataataata gatttttatta cgcgatcgat tattttatttc ctgaaaacaa 300  
ataaaaaaat ccccgccaaa tggcagggat cttagattct gtgcttttaa gcagagatt 359

<210> 58  
<211> 700  
<212> DNA  
<213> E. Coli

<220>  
<221> misc\_feature  
<222> (1)...(700)  
<223> n = A,T,C or G

<400> 58  
aaaccttttt ctccgtgtttt tcatagaggg caacccatgt cctgacctgg gtccggggga 60  
caccaaaacg tgccgagatg atccctgtaac catcatcagt tgtgaagtag tgattcacga 120  
cttcaaggcg cttttcaaaa gggatattttg gctttgacat attaggggct attccatttc 180  
atcgctcaac aaaatgggtg cagtacatac tcggttgaaa tcaacacagg aggctgggaa 240  
tgccgcagaa atatatagatta ctttcttttaa tagtgatttg tttcacgctt ttatttttca 300  
cctggatgat aagagattca ctgtgtgaat tgcattataa acaggagagt tatgagctgg 360  
cgccgttttt agcctgcaaa ttgaaagagt aagagtcttc ggcgggaaat tattcccgcc 420  
ttacttacgg cgttgccgat tctcattgca cccaaattta ttcttcacaa aaataataat 480  
agattttatt acgcgatcga ttattttatt cctgaaaaca aataanaaaa tccccgccaa 540  
atggcagggg tcttagattc tgtgctttta agcagagatt acaggctggg tacgttacca 600  
gctgccgggc cttaacgccc gctttcgatg gtgaaggaca ctttctgacc ttctgtccaga 660  
gattgtaacc atcgggtctgg atagccnaga aatgtccaac 700

<210> 59  
<211> 631  
<212> DNA  
<213> E. Coli

<220>  
<221> misc\_feature  
<222> (1)...(631)  
<223> n = A,T,C or G

<400> 59  
tggtggcatt gggtgctgga gagagaaaac ccccgccacgt tgcaggatat cacctgacaa 60  
caccacgggg gctaattctg actctagacc actcaagaat agccgcgaaa cgttgtcatt 120  
acaacacagg cggtatatat acgttcgcag agctgggcat ggccttctgg catgatttag 180  
cggctccggg cattgctggc attcttgcca gtatgatcgt gaactggctg aacaagcgga 240  
agtaacgtgt catgccccgg tcaggctgcc gtaatggcaa tttgcgccc gaccaggccg 300  
caggggggaa actctgcggc ctttttcgtt cttactgagg gtaaggcacc cagtcgccc 360  
cgttcaggcg aacgtacggg ttatcctggt attgaataac tactgcattt gagttctcgg 420  
agaccggtgc tgtttgtggc aaccactggt tgagtttttt ccagtcaaca ttgtcttcgg 480  
tgaaaatctt gccatcgaga acgcgaacca ccagatcgga gatagccagg aagctgctcg 540  
gttggtcgat gacaatcggg gccccctgat gcggtgcctt catgccgaag aatttcaccc 600  
caacgggggac gtcngtgata gaccgggcta g 631

<210> 60  
<211> 648  
<212> DNA  
<213> E. Coli

<220>  
<221> misc\_feature  
<222> (1)...(648)  
<223> n = A,T,C or G

<400> 60

ggctcaggcn	tgctgattgt	ttttttgtgc	aatggcccng	tattagcgctc	gttgctgtcg	60
atggagagaa	tcataaacgt	ggtgaatgat	gattgttagc	aaggaaaact	gtcaaaaatc	120
ttcaaaaaat	ttgagggata	aggccggaat	ggctccggcc	agaggggaagt	taaccgcgaa	180
gctgttgctg	cttgagggtc	gttttaacca	gacgccaggc	gctccatacg	ccaaaaccgc	240
gtctggccca	gcggaccagc	atattaggat	ggcgaatcgt	ccagatcgcc	atcacgctac	300
tgccaaccag	cgcccaggag	cgcagactta	gcagcatatt	ccancgacga	tcgtaagcgc	360
ctgttgcttc	cagccattca	cgacgactgg	cggaagggnc	cgcgntcgac	caacttgntc	420
tttagntcga	tncanattan	attnataaac	gcagnanncn	ggtntgatta	atcntatttn	480
gctctngtct	ggtagttagc	nncggnnngt	ctcntntna	cccnnttcnn	tttannttac	540
natnngtaan	tatatntnt	nngtctnant	tnntantgng	tactntaagt	ntatncgnnn	600
atnntnnnan	nnnncagunc	ntntttttta	aatnntttnt	nanncnnc		648

&lt;210&gt; 61

&lt;211&gt; 737

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(737)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 61

tgctaataatc	tttctcattg	agatgaaaat	taaggtaagc	gaggaaacac	accacacccat	60
aaacggaggc	aaataatgct	gggtaatatg	aatgttttta	tggccgtact	gggaataatt	120
ttattttctg	gtttttctggc	cgcgtatttc	agccacaaaat	gggatgacta	atgaacggag	180
ataatccctc	acctaaccgg	ccccttggtta	cagttgtgta	caaggggctt	gatttttatg	240
acggcgaaaa	aaaaccgcca	gtaaaccggc	ggtgaatgct	tgcatggata	gatttgtggt	300
ttgcttttac	gctaaccaggc	attttcctgc	actgataacg	aatcgttgac	acagtagcat	360
cagttttctc	aatgaatggt	aaacggagct	taaactcggg	taatcacatt	ttgttcgtca	420
ataaacatgc	agcgatttct	tccggtttgc	ttaccctcat	acattgccc	gtccgctctt	480
ccaatgacca	catccagagg	ctcttcagga	aatgcgcgac	tcacacctgc	tgtcacggta	540
atgttgatat	gcccttcaga	atgtgtgatg	gcattggttat	cgactaactg	gcaaattctg	600
acacctgcac	gacatgcttc	ttcatcatta	gccgctttga	caataatgat	aaattcttcg	660
cccccgtagc	gataaacccg	ttcgtaatna	cgcgtccaac	tgggntaagt	aaagttgcc	720
gggtgccgta	atctttac					737

&lt;210&gt; 62

&lt;211&gt; 648

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(648)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 62

tgcttttgaa	tatgtgctcg	caatcttgag	aaggaaatgg	cgaccacgaa	agaaaaggca	60
aaaaccgata	atctgaaaga	acccaagtat	ttcagtataa	gcattgaatg	ccgaccagta	120
aactctttcg	gattcaccca	gaaagtgaan	ccaaaatgat	aatcgtatac	ataagtcttt	180
cgagtggctc	gttagcaaaa	agtttcaaca	atggagtaaa	tacatccaac	atatcaataa	240
ctctcaactg	taaggggatt	gaaatggtaa	ccccagctct	tcgcttgagg	ggtatagccg	300
agaccacgga	agccccggag	gtggtgaaat	aaaaccgggc	acaacacgaa	agggcgcat	360
tccgatatcc	ataaaaagaag	tcgggtcttt	gtctggtaaa	attaaattgg	tgggaagtgc	420
gcctccgggt	tgtaaatacc	gacttttgctg	ggtgtagcct	ggcggcatca	agtttttttc	480
tgggaagtgc	ctgatgtccg	cccttttttaa	aggggaatttt	ggtgatgccg	gtgaatgccg	540
cttaaccccc	cgtggggcca	gttaaaaagtc	atggtaagnc	ctaattnggt	tgggggtggga	600
aaagccnact	gnnaattggt	tacctggttt	gcaagtancc	ctggaagg		648

&lt;210&gt; 63

<211> 237  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(237)  
 <223> n = A,T,C or G

<400> 63  
 ggtgtttant tacaagagat tcatctttgt ntaaancccn gataagtaat tacgcataaa 60  
 acaacaatga ttataatagc aaaaataaat attatcatct ttgatagatt acttgagata 120  
 gccagcatct tgtaaagcct ttatcgtttt tttatgctct ggattaatat aatcactaca 180  
 tctatctgag caatctgttg ttgatggaca tgtcaacca tggtcattta cagccaa 237

<210> 64  
 <211> 427  
 <212> DNA  
 <213> E. Coli

<400> 64  
 gataattaga gtttgcgctc agaaaattga cgttacccat aacaaatgaa aggccaggta 60  
 aatcatgcca ttatgcattg ttgctatcgg tgtaatcttg ttgttgctcc tgatgatccg 120  
 cttcaaaatg aacggcttca tcgctctcgt cctcgtggcg cttgctgttg gattaatgca 180  
 aggaatgccg ctggataaag ttattggctc catcaaaagcc ggtgtcggcg ggacgctcgg 240  
 tagccttgcc ctgatcatgg gttttggcgc aatgctgggc aaaatgctgg cagactgcgg 300  
 tggcgcacaa cgtatcgcca ccacgctgat tgccaaattt ggtaaaaaac acatccagtg 360  
 ggcggtggtg ctgaccggtt ttaccgttgg ttttgccctg ttctatgaag tgggctttgt 420  
 gctgatg 427

<210> 65  
 <211> 261  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(261)  
 <223> n = A,T,C or G

<400> 65  
 caaagaacct tcaacatgaa aaatatccat ttgtttgcaa aaaaagatta ttaggaagga 60  
 aattaatgca attatcgaaa attcaaaaaa tatccaaaaa tngtatactt tattccagaa 120  
 gagttcaata taatgtttgt cttcaatttt tcttacttca gggtaatata gattgctcat 180  
 tacattgtga gcttcatctt tatttaattt tctgttgact ccagctctcc gtgataacgg 240  
 ttttataatt agatgcttat c 261

<210> 66  
 <211> 98  
 <212> DNA  
 <213> E. Coli

<400> 66  
 agatgattgc cgggaacttg ttagcggcac gcaggcggcg gctcgcaccc ttaccctgct 60  
 ctttacgtac ttctgcgttg atagtaaaca tttctttc 98

<210> 67  
 <211> 260  
 <212> DNA  
 <213> E. Coli

&lt;400&gt; 67

aagcgcgaac	gaagtcgatg	tgctgcagct	tcggtttgta	cgggtgacgc	tgtacgtcct	60
gagcttttaac	tttgatttct	ttaccgtcaa	caacgatggt	cagaacttcg	ctgtagaatt	120
cagcttttagc	ttgcatgttc	atgactttgt	cgtgatccag	ctcgatagcc	agcggcgctt	180
ctttgccacc	gtagatgatt	gccgggaact	tgtagcggc	acgcaggcgg	cggctcgcac	240
ccttaccctg	ctctttacgt					260

&lt;210&gt; 68

&lt;211&gt; 95

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 68

aaaaacggcg	taaagaaagg	ttgcaaacat	gttaataaaa	actcaaattg	atcccacgta	60
tatattacgc	cgcaaaatcc	ttacaataaa	caggg			95

&lt;210&gt; 69

&lt;211&gt; 174

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 69

ttaattatta	aaatagtgtg	acgcgattat	gtggttatgg	gggtaaacat	taaataaacc	60
agcggggagg	ggaggtaaag	tgaaaaaata	aaaagcggat	aatcttaata	agcaggccgg	120
acagcatcgc	catccggcac	tgatacgagg	tttatttcag	ctcatcaacc	atcg	174

&lt;210&gt; 70

&lt;211&gt; 138

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 70

agtctgtaaa	aacgtcaaaa	agagtgtttt	atcaacagaa	gaatggaggt	ctgacagata	60
gtagtaatgc	aaaaaaatgg	agacttaagt	tgaatgaacg	ggagtaaagc	gaaaagacta	120
tagagtgaag	gagaaatt					138

&lt;210&gt; 71

&lt;211&gt; 191

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 71

tttgttggct	taatattcta	ttgttatctt	tatttataga	tgtttatatt	gcatgaggtg	60
gtttttggag	agaagaatga	ggaagatgcg	tcgagccaca	gaaacgtag	ctttacatat	120
agcggaggtg	atgtgaattt	aattttacaat	agaaataatt	tacatatcaa	acagttagat	180
gctttttgtc	g					191

&lt;210&gt; 72

&lt;211&gt; 244

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 72

ggccatttat	acaggaaaag	cctatgtcag	aacgtaaaaa	ctcaaaatca	cgccgtaatt	60
atctcgtaa	atgttcctgc	ccaaactgca	cccaagagtc	agaacacagt	ttttcaagag	120
tacaaaaagg	tgcccttttg	atctgccctc	attgcaacaa	agtattccag	acaaatctta	180
aagctgtagc	ctgattgatt	ttattagtaa	caagtatttt	ttatatatta	ataatatatt	240
taaa						244

&lt;210&gt; 73

&lt;211&gt; 327

<212> DNA  
<213> E. Coli

<220>  
<221> misc\_feature  
<222> (1)...(327)  
<223> n = A,T,C or G

<400> 73  
aaattttcag gtaccttgct accatacttt tttttctgag cattaatgat attttgagct 60  
tcttgaggat ctttaactcc ccacatttgg tggaaagtat tcatattaaa aggaaggntg 120  
aataatttgn ctttataaat cgccagtgga gaattagtaa aacgattaaa ttctactaaa 180  
tnattaaccg naaaaaaatt cccatatata tttatcattg gtatgaaaaa tatgtgcacc 240  
atatttatga atntggatac cctnacagtc ctctgtgtac gcatttccac cgatatgatt 300  
tcttttctna atcactaaaa cttttttt 327

<210> 74  
<211> 150  
<212> DNA  
<213> E. Coli

<400> 74  
gcagtgatcg aagcgatgac gaagtgtatg gaaaaatcag aaaaactcag caaatcctga 60  
tgactttcgc cggacgtcag gccgccactt cggtgcggtt acgtccggct ttctttgctt 120  
tgtaaagcgc caaatctgcc gatttcaacc 150

<210> 75  
<211> 330  
<212> DNA  
<213> E. Coli

<400> 75  
gaaagtatct tcgttattga catcaactgga aaatataact tgcttttcat tattaactc 60  
gaagcgcgta ccgtatctgg acaaacattt atcgagctta ccaaattcct gaagaggttt 120  
aactacagat aacatttgcg cgctctttgc agtaatgcc gtcaaattcct tgacgggcat 180  
tatttagatt aaattaccag tatttcttcg gagtgaagaa tattaccagg tatatttaac 240  
acccacgttc gcggaccagt cttgatctac gtcaccacca ccgaggtagt tagcatcggt 300  
ataggcgctg aagttcttgg tgaagctaaa 330

<210> 76  
<211> 194  
<212> DNA  
<213> E. Coli

<400> 76  
tgtttttttc cagcaacgga gcaaaagggt tgcccttgtg cagctcaggg ttaaccactt 60  
taactacgtg gcgacgaccc ggagatgtcg gtttacattt aacaactgcc attgtattac 120  
tcctccgact tactcagcgc cgccaacgaa gtccagattc tggccttctt tcagggtgac 180  
gtaagctttt ttcc 194

<210> 77  
<211> 188  
<212> DNA  
<213> E. Coli

<400> 77  
tccctttaac taccaggggtg ttaacgactt cgacttcgac ttcaaacagt ttctgcacag 60  
cagctttgat ttctgctttg gtcgcgtctt tagcaacttt gactactatg gtgttgatt 120  
tttccatcgc agtagacgct ttttcagaaa cgtgcggtgc acgcagcacc ttcagcagac 180  
gttcttca 188

<210> 78  
 <211> 173  
 <212> DNA  
 <213> E. Coli

<400> 78  
 acaaaggcga acaaagcctg tgaagcccga aggctccaca gacagtgcta cttgaaggcc 60  
 ttactgtttc ttcttaggag cgagcaccat gatcatctgg cggccttcga tcttggttgg 120  
 gaaggattcg accactgcca gttcttgcaa atcgtctttc acgcgattaa gca 173

<210> 79  
 <211> 272  
 <212> DNA  
 <213> E. Coli

<220>  
 <221> misc\_feature  
 <222> (1)...(272)  
 <223> n = A,T,C or G

<400> 79  
 tggagaaaac gggtgattga taaagcaatc atcgttctag gggcgttaat tgcgctgctg 60  
 gaactgatcc cgctttctgc ttcaagcttc tgaactggat acggaacgt aatnagggt 120  
 aaagaagaca ctactcttag ccctttaaca tttaacgcat tgtcacgaac tcttctgccg 180  
 ccgttggttg aatggcgacg ggtattggtc gaaatctttt ttgggtggcc ccattcttaa 240  
 cgcccaccgc cgaaaccctg caacatttcg tc 272

<210> 80  
 <211> 259  
 <212> DNA  
 <213> E. Coli

<400> 80  
 cgcaggcagc tgatgggtcaa caggatgaga gaaaccgaga gacagggttaa tcacattgcc 60  
 tttaaccgct gcacggtaac ctacaccaac cagctgcagc ttcttagtga agccttcggt 120  
 aacaccgata accattgagt tcagcagggc acgcgcggta ccagcctgtg cccaaccgtc 180  
 tgcgtaacca tcacgcggac cgaaggtcag ggtattatct gcatgtttaa cttcaacagc 240  
 atcgttgaga gtacgagtc 259

<210> 81  
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 <213> E. Coli

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 ccgtttaccg ggg 73

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 <212> DNA  
 <213> E. Coli

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agttaa						666

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 <212> DNA  
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<210> 84  
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 <212> DNA  
 <213> E. Coli

<400> 84						
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 <212> DNA  
 <213> E. Coli

<400> 85						
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&lt;210&gt; 86

&lt;211&gt; 1185

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 86

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&lt;210&gt; 87

&lt;211&gt; 2115

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 87

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&lt;210&gt; 88

&lt;211&gt; 540

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 88

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&lt;210&gt; 89

&lt;211&gt; 1549

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 89

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&lt;210&gt; 90

&lt;211&gt; 375

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 90

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&lt;210&gt; 91

&lt;211&gt; 366

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 91

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aaataa						366

&lt;210&gt; 92

&lt;211&gt; 498

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 92

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<210> 93  
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 <212> DNA  
 <213> E. Coli

<400> 93

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&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 95

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&lt;210&gt; 96

&lt;211&gt; 900

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 96

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&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 97

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&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 98

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 <211> 1536  
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<400> 99

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<400> 100

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&lt;213&gt; E. Coli

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&lt;210&gt; 102

&lt;211&gt; 1023

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 102

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&lt;210&gt; 103

&lt;211&gt; 876

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 103

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&lt;210&gt; 104

&lt;211&gt; 291

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 104

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&lt;210&gt; 105

&lt;211&gt; 1152

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 105

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&lt;210&gt; 106

&lt;211&gt; 3048

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 106

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&lt;210&gt; 107

&lt;211&gt; 885

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 107

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&lt;210&gt; 108

&lt;211&gt; 654

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 108

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&lt;210&gt; 109

&lt;211&gt; 261

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 109

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&lt;210&gt; 110

&lt;211&gt; 1203

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 110

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1203

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<210> 112  
 <211> 1326  
 <212> DNA  
 <213> E. Coli

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caatga						1326

<210> 113  
 <211> 585

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 113

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gaagagatca	tcgaatacgt	tcgtgttgcc	gcgctgttat	gccacgacac	ctttactcat	540
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&lt;210&gt; 114

&lt;211&gt; 363

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 114

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tcgactacaa	cgatgcgcta	catgctatat	gttgggttca	tggggacact	gagtgtact	240
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&lt;210&gt; 115

&lt;211&gt; 921

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 115

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&lt;210&gt; 116

&lt;211&gt; 1332

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 116

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gtaactttat	ttacattctt	tatttttagct	tttcttatgt	gttcttcatc	aacactgtca	420
atgtttgcat	cattctatca	agagcaaata	gttataattt	tccttccatt	tttggtgtat	480
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&lt;210&gt; 117

&lt;211&gt; 249

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 117

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&lt;210&gt; 118

&lt;211&gt; 183

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 118

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taa						183

&lt;210&gt; 119

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 119

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&lt;210&gt; 120

&lt;211&gt; 741

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 120

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&lt;210&gt; 121

&lt;211&gt; 1395

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 121

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&lt;210&gt; 122

&lt;211&gt; 3123

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 122

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taa						3123

&lt;210&gt; 123

&lt;211&gt; 3078

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 123

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&lt;210&gt; 124

&lt;211&gt; 1416

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 124

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&lt;210&gt; 125

&lt;211&gt; 1035

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 125

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&lt;210&gt; 126

&lt;211&gt; 2481

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 126

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&lt;210&gt; 127

&lt;211&gt; 720

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 127

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&lt;210&gt; 128

&lt;211&gt; 543

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 128

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taa

543

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 <212> DNA  
 <213> E. Coli

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 <212> DNA  
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 <212> DNA  
 <213> E. Coli

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<210> 132  
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 <212> DNA  
 <213> E. Coli

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&lt;210&gt; 133

&lt;211&gt; 1059

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 133

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&lt;210&gt; 134

&lt;211&gt; 621

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 134

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&lt;210&gt; 135

&lt;211&gt; 696

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 135

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&lt;210&gt; 136

&lt;211&gt; 636

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 136

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&lt;210&gt; 137

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 137

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&lt;210&gt; 138

&lt;211&gt; 531

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 138

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&lt;210&gt; 139

&lt;211&gt; 1149

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 139

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&lt;210&gt; 140

&lt;211&gt; 417

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 140

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agcagcaatg	gctacacgct	ccccagagca	aactatttta	accactgtag	ttcccgaggc	6960
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ctggcaacag	gtgatcaaag	cgtatttgaa	aagcttgggt	ttgcttatgc	gacatgttat	7140
aaaaacctgt	ga					

7152

&lt;210&gt; 143

&lt;211&gt; 186

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 143

atgagcaaa	g	gcg	caattata	tgaatttaac	aatccagatc	aactgaaaat	acctctccct	60
cataaacaca	tag	cg	tcaac	attcaatgac	ataatgagta	aagatgttg	ttatgcatac	120
gtatcattac	tct	atg	cctg	tcccttaaaa	acccactcat	taagactgaa	tccattcagc	180
aatga								186

&lt;210&gt; 144

&lt;211&gt; 1197

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 144

atgcaggttg	ctgaacagcg	cattcagcta	gctgaagccc	aggcgaaggc	agttgccact	60
caggatgggtc	cgcatatcga	cttttcggcg	gatatggagc	ggcaaaaaat	gtcggcagaa	120
ggcttaaatgg	ggccgtttgc	tctgaacgat	ccggccgcag	gtacgaccgg	cccgtgggtac	180
accaacggta	cttttggtct	aacggcgggc	tggcatctcg	atatctgggg	aaagaatcgg	240
gcggagggtta	ctgcccgcct	gggtacgggt	aaagcacggg	cgccggaacg	cgagcaaacc	300
cgccaattgc	tggctggcag	cgtagcccg	ctgtactggg	agtggcaaac	ccaggcgggc	360
ttaaacaacgg	tcttgacgca	aatagaaaaa	gagcagaaca	ccattatcgc	gaccgatcgc	420
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aaagtggcaa	gccagcttcc	tgatgaactg	gggtactcct	tactggcccg	gcgggcagat	660
ttgcaggcg	cgactggta	cgttgagtc	tgcctaagca	ccattgatgc	ggcaaaagcg	720
gcattttatc	ctgacatcaa	cctgatggcc	ttcctgcaac	aggatgcgtt	gcacttaagc	780
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caggttcaga	cactggcgga	gaaaaaccag	catcaggcgc	aaattgagcg	cgatgccttg	1020
cgtgtggtag	gtcttgcgca	ggcgcgcttt	aacgcgggca	tcattgctgg	ttcccgcgctc	1080
agcgaagcca	gaatccccgc	gctgcgtgag	cgggccaatg	gcctgttatt	gcaaggcgag	1140
tggctggatg	cctccattca	actcactggg	gcgttgggcg	gggggtacaa	acgctga	1197

&lt;210&gt; 145

&lt;211&gt; 291

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 145

atgtattgcc	acgcgaaact	aaaaaatata	tcgcaacaca	cggtaatctc	cgcgcaacctt	60
ttcttacctg	attattcccc	catgaatcgt	gattccctttt	atccagccat	cgctgtttt	120
ccgctgttac	tgatgctggc	cggtgtgtgc	cctatgcatg	aaacccgcca	ggcgttaagc	180
cagcaaacgc	ccgctgcaca	agttgacacc	gcattaccca	cggcgctgaa	aatggttggc	240
cagacagcca	atggtggctg	gagtatcacg	ataatcaact	cacttcctta	a	291

&lt;210&gt; 146

&lt;211&gt; 948

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 146

atgctgtgtg	tactggcacc	gatggagggg	gtgcttgact	ctctggtgcg	tgaattgctg	60
accgaagtta	acgactacga	tctgtgcac	accgagtttg	tccgcgtggg	ggatcaactg	120
ctgccggtaa	aagtctttca	tcgcatttgc	cctgagctac	aaaacgccag	ccggacacca	180
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aaaacggtta	acggtagcgg	cggcggggcg	acgttactca	aagatcctga	actcatctac	360
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cgtaaagaat	acgatgaagc	aacggaatta	tttcagcatg	ttcgggtggt	gaataattcc	900
cctgatattg	caagggctat	tcaggcaatt	gatatcgaga	aactctaa		948

&lt;210&gt; 147

&lt;211&gt; 891

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 147

atgacaatat	cgacaacttc	cacgccgcat	gatgcgggtat	ttaaatcttt	tttacgccat	60
ccagacaccg	cgcgggattt	tattgatatt	catcttcccg	cgccgctgcg	caaactgtgt	120
gatttaacga	cgcttaaact	ggaaccaaac	agttttattg	atgaagacct	gcggcaatat	180
tattccgacc	tcttgtggtc	tgtgaaaacg	caggagggag	tgggttatat	ttatgtagtg	240
atagagcacc	aaagtaagcc	ggaagaatta	atggcttttc	gcatgatgcg	ttattccatt	300
gcggcaatgc	aaaaccatct	tgatgcgggc	tataaagagc	ttccattggg	gctcccagtg	360
ctgtttttatc	atggtttgcag	aagtccttat	ccttattcac	tctgctgggt	tgatgaattt	420
gccgagcctg	ctatagcccg	caaaatatat	tcatcggtt	ttccgttggg	ggatattacc	480
gtggtgccgg	atgacgagat	tatgcaacac	cgcaaaatgg	cgctgttgga	gttaattcag	540
aaacatatct	gtcagcgcga	tctgttgga	ttagtcgacc	aaattgtttc	gctgctagtt	600
acagggaaaca	ctaattgacag	acagctaaaa	gccctgttta	attacgtatt	acaaacaggg	660
gatgcccagc	gttttcgtgc	atttattggg	gagatagcgg	aacgcgcacc	acaagaaaag	720
gagaaactga	tgaccattgc	tgacagatta	cgtgaagaaag	gcgcaatgca	gggcaaacac	780
gaagaagccc	tgcttattgc	tcaggagatg	ctggatagag	gtttagacag	agagttagtt	840
atgatgggtga	cccgaacttc	accagacgat	cttatcgcg	aaagccacta	a	891

&lt;210&gt; 148

&lt;211&gt; 1668

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 148

gtggctcaat	tcgtttatac	catgcatcgt	gtcggcaaag	ttgttccgcc	gaaacgtcat	60
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attttgaaaa	acatctctct	gagtttcttc	cctggggcaa	aaattggtgt	cctgggtctg	120
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cgcgcgctgg	aaaacgccct	gctggagttc	ccgggctgtg	cgatggttat	ctcgcacgac	1500
cgttggttcc	tcgaccgtat	cgccacgcac	attctggatt	accaggatga	aggtaaagtt	1560
gagttcttcg	aaggtaactt	taccgagtac	gaagagtaca	agaaacgcac	gctgggcgca	1620
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&lt;210&gt; 149

&lt;211&gt; 522

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 149

atgtcaaagc	caaaataccc	ttttgaaaag	cgccttgaag	tcgtgaatca	ctacttcaca	60
actgatgatg	gttacaggat	catctcggca	cgttttggtg	tccccgaac	ccaggtcagg	120
acatgggttg	cctctatga	aaaacatgga	gaaaaggtt	taattcccaa	acctaaaggc	180
gttagtgctg	atccagagtt	gcgtattaa	gtcgtgaaag	ctgtgatcga	gcagcacatg	240
tcccttaatc	aggctgctgc	tcactttatg	cttgctggta	gtggttctgt	agccaggtgg	300
ctgaaggtct	atgaagagcg	cggagaagct	ggtttacgcg	cgctcaagat	tggcaccaaa	360
agaaacattg	caatatcagt	tgatccagaa	aaagcggcat	cagcatttga	gctgtcaaaa	420
gaccgacgca	ttgaggatct	tgaaggcga	gttcgatttc	ttgaaacgcg	gcttatgtat	480
ctaaaaaagc	tgaagccctt	agctcatccc	acgaaaaagt	ga		522

&lt;210&gt; 150

&lt;211&gt; 852

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 150

gtgaaagtac	tcaacgagct	aaggcagttt	tatcctcttg	atgagcttct	cagggctgcg	60
gagataccgc	gcagtaagtt	ttattatcat	ctaaaggctc	tcagcaagcc	tgacaagtat	120
gcggaggtta	aaaagcgtat	tagtgagatt	tatcacgaga	atagaggccg	atacggatac	180
cgtagggttaa	cgtgtctct	tcactcgagaa	gggaaacaga	ttaaccataa	agctgttcag	240
cgcctgatgg	gaaccctctc	acttaaaagca	gcgattaaag	tcaagcgata	ccgtctctac	300
agaggagagg	tagggcaaac	cgcccttaat	gttctccaaa	gagatttcaa	ggctacgcgg	360
ccaaacgaga	agtgggttac	cgatgttact	gaatttgcag	tcaatgggcy	caagctgtat	420
ttgtctccag	taatagatct	cttcaacaac	gaagttatct	cttacagcct	ttcggaagaa	480
ccagtgtatga	acatgggttg	gaatatgctc	gatcaggcat	tcaaaaagct	taatcctcac	540
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agaattagcc	tgaaattaaa	aggctctgact	ccaattgaat	atcggaatca	gacctatatg	840
cctcgtgttt	aa					852

&lt;210&gt; 151

&lt;211&gt; 117

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 151

atgaaagtgc	gtgcttccgt	caagaaatta	tgccgttaact	gcaaaatcgt	taagcgtgat	60
gggtgcatcc	gtgtgatttg	cagtgccgag	ccgaagcata	aacagcgcca	aggctga	117

&lt;210&gt; 152

&lt;211&gt; 1332

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 152

atggctaaac	aaccgggatt	agattttcaa	agtgccaaag	gtggcttagg	cgagctgaaa	60
cgcagactgc	tgtttggtat	cggtgcgctg	attgtgttcc	gtattggctc	ttttattccg	120
atccctggta	ttgatgccgc	tgtacttgcc	aaactgcttg	agcaacagcg	aggcaccatc	180
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cagagcacac	atttaccgct	gaaagtgaat	atggcggggg	taatccccgc	aatcttcgct	840
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aactggctga	caacaatttc	gctgtatttg	cagcctgggc	aaccgcttta	tgtgttactc	960
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caaactctga	tgatgtccag	tcagtatgag	tctgcattga	agaaggcgaa	cctgaaaggc	1320
tacggccgat	aa					1332

&lt;210&gt; 153

&lt;211&gt; 435

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 153

atgcgtttta	atactctgtc	tccggccgaa	ggctccaaaa	aggcgggtaa	acgcctgggt	60
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&lt;210&gt; 154

<211> 180  
 <212> DNA  
 <213> E. Coli

<400> 154

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actcctgcta	ttcgcggtat	gatcaacgcg	gttccttca	tggttaaagt	tgaggagtaa	180

<210> 155  
 <211> 504  
 <212> DNA  
 <213> E. Coli

<400> 155

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gttgaagaaa	ttctggggaa	ataa				504

<210> 156  
 <211> 354  
 <212> DNA  
 <213> E. Coli

<400> 156

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ggcgtgttcc	aggcactggc	agatgctgcc	cgtgaagctg	gccttcagtt	ctaa	354

<210> 157  
 <211> 534  
 <212> DNA  
 <213> E. Coli

<400> 157

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gttgaagtta	aacatgcaga	taataccctg	accttcgggtc	cgcgtgatgg	ttacgcagac	180
ggttgggcac	aggctggtac	cgcgcgtgcc	ctgctgaact	caatggttat	cggtgttacc	240
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aatgtgatta	acctgtctct	gggtttctct	cacctgttgc	accatcagct	gcctgcgggt	360
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ggtgttcgtt	acgccgacga	agtcgtgcgt	accaaagagg	ctaagaagaa	gtaa	534

<210> 158  
 <211> 393  
 <212> DNA  
 <213> E. Coli

<400> 158

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cttggtggcg	aaattatctg	ctacgtagcc	taa			393

&lt;210&gt; 159

&lt;211&gt; 306

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 159

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tggtaa						306

&lt;210&gt; 160

&lt;211&gt; 540

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 160

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&lt;210&gt; 161

&lt;211&gt; 315

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 161

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gaccgtgtag	gcttttagatt	cgaagacggt	aaaaaagtc	gtttcttcaa	gtctaacagc	300
gaaactatca	agtaa					315

&lt;210&gt; 162

&lt;211&gt; 372

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 162

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gaagtactct aa

372

<210> 163  
 <211> 567  
 <212> DNA  
 <213> E. Coli

&lt;400&gt; 163

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ccttgtagaa	ttcatccaga	agatattgat	aaaaacatag	atcttgga	agtcacgaca	180
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tcagccgcgc	cagatcttga	cctggatgca	agctcatcag	aacagacgct	gaactttttc	480
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gcaacctacg	tgctggatta	taaataa				567

<210> 164  
 <211> 1284  
 <212> DNA  
 <213> E. Coli

&lt;400&gt; 164

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tttaaaagcg	atatcaagcg	ttaa				1284

<210> 165  
 <211> 1434  
 <212> DNA  
 <213> E. Coli

&lt;400&gt; 165

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&lt;210&gt; 166

&lt;211&gt; 2841

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 166

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&lt;210&gt; 167

&lt;211&gt; 1302

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 167

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&lt;210&gt; 168

&lt;211&gt; 213

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 168

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ggcccggcag	ctggtaacgt	aaccagcctg	ttaa			213

&lt;210&gt; 169

&lt;211&gt; 1572

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 169

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cgctcatcat	ga					1572

&lt;210&gt; 170

&lt;211&gt; 189

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 170

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aaacctcggt	atgttaaacc	ggccgggacg	ttacgcgcga	cgaaaaaagc	cagggcaacc	180
aaaaaatga						189

&lt;210&gt; 171

&lt;211&gt; 1680

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 171

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&lt;210&gt; 172

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 172

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agctatgccg	aaaaacacca	aaaccagaat	cgtattgacg	gtctgaataa	agccctgagt	180
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aagcagaaa	atgaggtggc	ggaacgccag	caagatttag	ccgaggcgaa	gcaaaaaggc	300
gatgccgata	agattgccaa	acgcgaacgg	aaactggcag	aagcgcagga	agagctgaaa	360
aagctggaag	cgcgcgacta	ctaa				384

&lt;210&gt; 173

&lt;211&gt; 306

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 173

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attgccaaac	aaaccgcgtg	cgcgggcgcg	cgtgccgatg	agtatgtgcg	cgaaaatccg	240
tggacgggg	tgggcattgg	cgctgcaatc	ggtgtagtgc	tcggcgttct	gctgtcgcgt	300
cgtaa						306

&lt;210&gt; 174

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 174

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&lt;210&gt; 175

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 175

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<210> 176  
<211> 483  
<212> DNA  
<213> E. Coli

<400> 176

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ttaa						483

<210> 177  
<211> 891  
<212> DNA  
<213> E. Coli

<400> 177

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<210> 178  
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<212> DNA  
<213> E. Coli

<400> 178

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<210> 179  
<211> 177  
<212> DNA

&lt;213&gt; E. Coli

&lt;400&gt; 179

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&lt;210&gt; 180

&lt;211&gt; 4281

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 180

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&lt;210&gt; 181

&lt;211&gt; 369

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 181

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agtaataaa						369

&lt;210&gt; 182

&lt;211&gt; 711

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 182

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caggggcggt	atatcactca	ggacccgata	gggctggagg	ggggatggag	tctgtatgcg	240
tatccgctga	atccggtgaa	tggtattgat	ccattagggg	taagtcccgc	agatgtagcg	300
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&lt;210&gt; 183

&lt;211&gt; 261

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 183

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aaacattaca	taaactatat	ggcaatacca	gaaaatgatg	gagtttttac	atggctccca	180
gatttttttc	cgcacgtagc	ggtggatata	tcaatatata	caaagttaga	agatgattat	240
ttttttctta	tttttccta	a				261

&lt;210&gt; 184

&lt;211&gt; 192

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 184

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tgtgcagagt	aa					192

&lt;210&gt; 185

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 185

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ctgaacataa	aacactatca	ataa				504

&lt;210&gt; 186

&lt;211&gt; 276

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 186

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&lt;210&gt; 187

&lt;211&gt; 417

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 187

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agaaataatg	atgatttcat	aaaccctgat	ctacaagaac	ggtagtgat	cggggattat	360
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 <212> DNA  
 <213> E. Coli

<400> 188

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 <211> 666  
 <212> DNA  
 <213> E. Coli

<400> 189

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atataa						666

<210> 190  
 <211> 705  
 <212> DNA  
 <213> E. Coli

<400> 190

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tcgataattg	cattaatttc	cttcctaata	atcttttttt	gcaaacaaat	ggatattttt	540
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ggtattatct	ttgctttgac	agttaagccc	agaactgaaa	gtcaagtcgg	aaaaatcccc	660
gacgataaaa	taaaagaatt	tttcaactaaa	aataacatta	attga		705

&lt;210&gt; 191

&lt;211&gt; 285

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 191

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&lt;210&gt; 192

&lt;211&gt; 1977

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 192

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&lt;210&gt; 193

&lt;211&gt; 2634

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 193

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tgctcagaaa	cgatgatgga	tgaacacatt	accaccgagg	aaaatcaagg	ttcaaatcta	2580
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&lt;210&gt; 194

&lt;211&gt; 1572

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 194

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ggcccaagca	gcctgaaaac	cggtcgctat	cactttgagc	agtcttccac	gactactcag	1560
ccggcacgct	aa					1572

&lt;210&gt; 195

&lt;211&gt; 1140

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 195

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cgtaacgaca	ccgagcgctg	aattatgatt	aactccattg	caccacactg	ggacggtaac	180
caggtttggc	tgatcaccgc	ggcgccgcga	ctctttgctg	cctggccgat	ggtctatgcc	240
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&lt;210&gt; 196

&lt;211&gt; 1371

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 196

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agcgcgctgc	gcgggatttt	cagcgaaatat	ggtttgctga	aattccgtgt	acaagttgaa	120
gtacgtttggc	tgcaaaaact	ggccgcgcac	gcagcgatca	aggaaattcc	tgcttttgct	180
gccgacgcaa	tcggttacct	tgatgcaatc	gtcgccagtt	tcagcgaaga	agatgcggcg	240
cgcatacaaaa	ctatcgagcg	taccactaac	cacgacgtta	aagcggttga	gtatttccctg	300
aaagaaaaag	tggcggagat	cccggaaactg	cacgcggttt	ctgaattcat	ccactttgcc	360
tgtacttcgg	aagatatcaa	taacctctcc	cacgcattaa	tgctgaaaac	cgcgcgtgat	420
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cagtttatcg	atgggtctggc	gttgccagaa	gaagagaaaag	ccgcctgaa	agcgtgacg	1320
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&lt;210&gt; 197

&lt;211&gt; 186

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 197

atgctgattc	tgactcgctg	agttggtgag	accctcatga	ttggggatga	ggtcaccgtg	60
acagttttag	gggtaaagg	caaccaggta	cgtattggcg	taaatgcccc	gaaggaggtt	120
tctgttcacc	gtgaagagat	ctaccagcgt	atccaggctg	aaaaatcccc	gcagtcacgt	180
tactaa						186

&lt;210&gt; 198

&lt;211&gt; 93

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 198

ggtgagggtg	ccgagaggct	gaaggcgctc	ccctgctaag	ggagtatgcg	gtcaaaagct	60
gcatccgggg	ttcgaatccc	cgcctcaccg	cca			93

&lt;210&gt; 199

&lt;211&gt; 603

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 199

atgaagaata	aggctgataa	caaaaaaagg	aacttcctga	cccatagtga	aatcgaatca	60
ctccttaaag	cagcaaatat	cgggcctcat	gcagcacgta	attattgtct	gactttgctt	120
tgttttattc	atggtttccg	ggcgagtga	atttgctgat	tgaggatttc	ggatattgat	180
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ctattgaata	aagaagttca	ggctttaaaa	aactgggtga	gtatccgtac	ttcgtacccg	300
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cacatgttac	gccattcgtg	tggttttgct	ttggcgaaata	tggaataga	tacgcgactt	480
atccaggatt	atcttgggca	tcgcaatatt	cgtcatactg	tctggtatac	cgccagcaat	540
gcagggcgtt	tttacggcat	ctgggataga	gccagaggac	gacagcgtca	cgtgttttta	600
tag						603

&lt;210&gt; 200

&lt;211&gt; 597

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 200

gtgagtaaac	gtcgttatct	taccggtaaa	gaagttcagg	ccatgatgca	ggcggtttgt	60
tacggggcaa	cgggagccag	agattattgt	cttattctgt	tggcataatc	gcattgggatg	120

cgtatttagtg	aactgcttga	tctgcattat	caggaccttg	accttaaatga	aggtagaata	180
aatattcgcc	gactgaagaa	cggattttct	accgttcacc	cgttacgttt	tgatgagcgt	240
gaagccgtgg	aacgctggac	ccaggaacgt	gctaactgga	aaggcgctga	ccggactgac	300
gctatatatta	tttctcgccg	cgggagtcgg	ctttctcgcc	agcaggccta	tcgcattatt	360
cgcgatgccg	gtattgaagc	tggaaaccga	acgcagactc	atcctcatat	gttaaggcat	420
gcttgcggtt	atgaattggc	ggagcggtgt	gcagatactc	gtttaattca	ggattatctc	480
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ggattatggg	aaagaaataa	tctcataaac	gaaaaattaa	aaagagaaga	ggtttga	597

&lt;210&gt; 201

&lt;211&gt; 549

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 201

atgaaaatta	aaactctggc	aatcggtgtt	ctgtcggctc	tgtccctcag	ttctacagcg	60
gctctggccg	ctgccacgac	ggttaatggt	gggaccgttc	actttaaagg	ggaagtgtgt	120
aacgccgctt	gcgcagttga	tgcaggctct	ggtgatcaaa	ccgttcagtt	aggacagggt	180
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aacgttggtg	tgcagatcct	ggacagaacg	ggtgctgcgc	tgacgctgga	tggtgcgaca	420
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tatcaataa						549

&lt;210&gt; 202

&lt;211&gt; 648

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 202

gtgctgctaa	tgcggatgcg	accttcaagg	ttcagtatca	ataacctacc	caggttcagg	60
gacgtcatta	cgggcaggga	tgccaccctt	tgtgcgataa	aaataacgat	gaaaagggaag	120
agattatttc	tattagcgtc	gttgctgcca	atgtttgctc	tggccggaaa	taaatggaat	180
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ggcggcatcg	ccaatgccca	ggcctggttc	tctttaacct	atcagtaa		648

&lt;210&gt; 203

&lt;211&gt; 726

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 203

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ggtatcctga	tgttcattggc	aatgatggtt	gccggacgcg	ctgaagcggg	agtggcctta	120
ggtgcgactc	gcgtaattta	tccggcaggg	caaaaacaag	agcaacttgc	cgtgacaaat	180
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gcattgggtg	ctccaatggg	cgaagcacg	gttaaatgtc	cttctgatgc	aggaagcaat	660

attactttacc gaacaataaa tgattatggc gcactttacc ccaaaatgac gggcgtaatg 720  
gaataa 726

&lt;210&gt; 204

&lt;211&gt; 2637

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 204

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catcggttgg ctgggttttt tgtccgactc gttgtgcct gtgcttttgc cgcacaggca 120  
cctttgtcat ctgccgacct ctatttttaat ccgcgctttt tagcggatga tccccaggct 180  
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gatatctatt tgaataatgg ttatatggca acgcgatgat tcacatttaa tacgggagac 300  
agtgaacaag ggattgttcc ctgcctgaca cgcgcgcaac tcgccagtat ggggctgaat 360  
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cgtttacgcg acaataccac ctggagttat aacagtagcg acagatcatc aggtagcaaa 720  
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ggaaaagtgc aggtgaaatg gggagaagag gaaaatgctc actgtgtcgc caattatcaa 2580  
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&lt;210&gt; 205

&lt;211&gt; 531

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 205

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aacattggcg	cgacgactcc	tgttggtcca	tttcgtat	tgctgtcacc	ctgtggtaat	240
gccgtttctg	ccgtaaaggt	tgggtttact	ggcgttgacg	atagccacaa	tgccaacctg	300
cttgcaactg	aaaatacgg	gtcagcggct	tcgggactgg	gaatacagct	tctgaatgag	360
cagcaaaatc	aaatacccct	taatgctcca	tcgtccgcgc	tttcgtggac	gaccctgacg	420
ecgggtaaac	caaatacgg	gaatttttac	gcccggctaa	tggcgacaca	ggtgcctgtc	480
actgcggggc	atatcaatgc	cacggctacc	ttcactcttg	aatatcagta	a	531

&lt;210&gt; 206

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 206

atgaaatggt	gcaaacgtgg	gtatgtattg	gcggcaatat	tggcgctcgc	aagtgcgacg	60
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gtttccacca	ccaatgccac	ggttgatctc	ggcgatcttt	attctttcag	tcttatgtct	180
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&lt;210&gt; 207

&lt;211&gt; 903

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 207

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&lt;210&gt; 208

&lt;211&gt; 1631

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 208

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&lt;210&gt; 209

&lt;211&gt; 534

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 209

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&lt;210&gt; 210

&lt;211&gt; 312

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 210

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&lt;210&gt; 211

&lt;211&gt; 291

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 211

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 <213> E. Coli

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 ggctttggtc ataataataa tattgcggtg gcgtatgtaa aggaaaaata tagacccgca 240  
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&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 216

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&lt;210&gt; 217

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&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 217

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&lt;210&gt; 218

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&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 218

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&lt;212&gt; DNA

&lt;213&gt; E. Coli

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&lt;213&gt; E. Coli

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&lt;210&gt; 221

&lt;211&gt; 1404

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 221

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&lt;210&gt; 222

&lt;211&gt; 669

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 222

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caggctcctt	atattatggg	gctggctgat	ggtttaatga	aaaacgatat	accatacaaa	300
ttaatatcag	aaggaaattg	tacgggatat	catctaccag	ccaaacaaac	cattacgctt	360
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gagtattaa						669

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 <213> E. Coli

<400> 223						
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acgaccaaac	tgcacgtaca	tgacgagaac	aacgaatgcg	gtatcggtga	cgtgggtgaa	180
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aaagcggttc	tgtaa					255

<210> 224  
 <211> 192  
 <212> DNA  
 <213> E. Coli

<400> 224						
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gcgggtgcgt	aa					192

<210> 225  
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 <212> DNA  
 <213> E. Coli

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gcgcagggtg	cggatgttag	cttcggcagc	ttcgggtctga	aagctgttgg	ccgtgggtcgt	120
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cgtatgggta	aaggtaaaag	taacgtggag	tattgggttg	ccttgattca	gccgggtaaa	300
gtcctgtatg	aaatggacgg	tggtccggaa	gagctggccc	gtgaagcatt	caagctggca	360
gcagcgaaac	tgccgattaa	aaccaccttt	gtaactaaga	cggtgatgta	a	411

<210> 226  
 <211> 702  
 <212> DNA  
 <213> E. Coli

<400> 226						
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gctaagagca	tccgtgtaac	cattcacact	gctcgcccgg	gtatcgttat	cggtaaaaaa	240
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<210> 227

<211> 333  
 <212> DNA  
 <213> E. Coli

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<210> 228  
 <211> 279  
 <212> DNA  
 <213> E. Coli

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 tttcctaaca tgatcgggtt gaccatcgct gtccataatg gtcgtcagca cgttccggta 180  
 tttgtaaccg acgaaatggg ttgtcacaaa ctgggtgaat tcgcaccgac tcgtacttat 240  
 cgcgccacg ctgctgataa aaaagcgaag aagaaataa 279

<210> 229  
 <211> 822  
 <212> DNA  
 <213> E. Coli

<400> 229  
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 aaccttgagc tgcacaaggg caaacctttt gctccgttgc tggaaaaaaa cagcaaatcc 120  
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 gcttaccgta ttgttgactt caaacgcaac aaagacggta tcccggcagt tgttgaacgt 240  
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 cgccgttaca tcctggcccc taaaggcctg aaagctggcg accagattca gtctggcggt 360  
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 aagcgtactg ataaattcat cgtacgtcgc cgtagcaaat aa 822

<210> 230  
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 <212> DNA  
 <213> E. Coli

<400> 230  
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 gcagaaatca aagctgctgt gcagaaactg tttgaagtcg aagtcgaagt cgttaacacc 180  
 ctggtagtta aagggaaagt taaacgtcac ggacagcgta tcggtcgtcg tagcgactgg 240  
 aaaaaagctt acgtcaccct gaaagaaggc cagaatctgg acttcgttgg cggcgctgag 300  
 taa 303

<210> 231  
 <211> 630  
 <212> DNA

&lt;213&gt; E. Coli

&lt;400&gt; 231

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&lt;210&gt; 232

&lt;211&gt; 606

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 232

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gcatga						606

&lt;210&gt; 233

&lt;211&gt; 312

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 233

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&lt;210&gt; 234

&lt;211&gt; 357

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 234

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&lt;210&gt; 235

&lt;211&gt; 198



&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 235

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&lt;210&gt; 236

&lt;211&gt; 543

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 236

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taa						543

&lt;210&gt; 237

&lt;211&gt; 1929

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 237

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 <212> DNA  
 <213> E. Coli

<400> 238

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<210> 239  
 <211> 2904  
 <212> DNA  
 <213> E. Coli

<400> 239

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agctaccggg	cagtgccatt	ggcatgacaa	ccgaaacacc	agtgatgcgt	ccactccggt	240
cctctcgtag	taggagcagc	ccccctcagt	tctccagcgc	ccacggcaga	tagggaccga	300
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ccttgggacc	tacttcagcc	ccaggatgtg	atgagccgac	atcgaggtgc	caaacaccgc	420
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ccaggattag	ccaaccttcg	tgctcctccg	ttactcttta	ggaggagacc	gccccagtca	660
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gctggatatct	tcgactgatt	tcagctccat	ccgcgaggga	cctcacctac	atatcagcgt	1200

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ccgtgtacgc	ttagtcgctt	aacc				2904

&lt;210&gt; 240

&lt;211&gt; 120

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 240

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&lt;210&gt; 241

&lt;211&gt; 76

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 241

gtcccccttcg	tctagaggcc	caggacaccg	ccctttcacg	gcggtaacag	gggttcgaat	60
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&lt;210&gt; 242

&lt;211&gt; 1549

&lt;212&gt; DNA

&lt;213&gt; E. Coli

&lt;400&gt; 242

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aatgtcgcaa	gaccaaagag	ggggaccttc	gggcctcttg	ccatcggtatg	tgcccagatg	240
ggattagctt	gttggtgggg	taacggctca	ccaaggcgac	gatccctagc	tggtctgaga	300
ggatgaccag	ccacactgga	actgagacac	ggtccagact	cctacgggag	gcagcagtg	360
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acaaggtaac cgtaggggaa cctgcggttg gatcacctcc ttaccttaa 1549

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&lt;210&gt; 243

&lt;211&gt; 221

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 243

```

Met Asn Val Phe Ser Gln Thr Gln Arg Tyr Lys Ala Leu Phe Trp Leu
1          5          10          15
Ser Leu Phe His Leu Leu Val Ile Thr Ser Ser Asn Tyr Leu Val Gln
20~        25        30
Leu Pro Val Ser Ile Leu Gly Phe His Thr Thr Trp Gly Ala Phe Ser
35        40        45
Phe Pro Phe Ile Phe Leu Ala Thr Asp Leu Thr Val Arg Ile Phe Gly
50        55        60
Ala Pro Leu Ala Arg Arg Ile Ile Phe Ala Val Met Ile Pro Ala Leu
65        70        75        80
Leu Ile Ser Tyr Val Ile Ser Ser Leu Phe Tyr Met Gly Ser Trp Gln
85        90        95
Gly Phe Gly Ala Leu Ala His Phe Asn Leu Phe Val Ala Arg Ile Ala
100       105       110
Thr Ala Ser Phe Met Ala Tyr Ala Leu Gly Gln Ile Leu Asp Val His
115       120       125
Val Phe Asn Arg Leu Arg Gln Ser Arg Arg Trp Trp Leu Ala Pro Thr
130       135       140
Ala Ser Thr Leu Phe Gly Asn Val Ser Asp Thr Leu Ala Phe Phe Phe
145       150       155       160
Ile Ala Phe Trp Arg Ser Pro Asp Ala Phe Met Ala Glu His Trp Met
165       170       175
Glu Ile Ala Leu Val Asp Tyr Cys Phe Lys Val Leu Ile Ser Ile Val
180       185       190
Phe Phe Leu Pro Met Tyr Gly Val Leu Leu Asn Met Leu Leu Lys Arg
195       200       205
Leu Ala Asp Lys Ser Glu Ile Asn Ala Leu Gln Ala Ser
210       215       220

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&lt;210&gt; 244

&lt;211&gt; 203

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 244

```

Met Ile Arg Trp Met Asn Glu Pro Leu Trp Pro Phe Ile Glu Arg Lys
 1           5           10           15
Lys Ser Met Arg Asn Leu Val Lys Tyr Val Gly Ile Gly Leu Leu Val
          20           25           30
Met Gly Leu Ala Ala Cys Asp Asp Lys Asp Thr Asn Ala Thr Ala Gln
          35           40           45
Gly Ser Val Ala Glu Ser Asn Ala Thr Gly Asn Pro Val Asn Leu Leu
          50           55           60
Asp Gly Lys Leu Ser Phe Ser Leu Pro Ala Asp Met Thr Asp Gln Ser
65           70           75           80
Gly Lys Leu Gly Thr Gln Ala Asn Asn Met His Val Trp Ser Asp Ala
          85           90           95
Thr Gly Gln Lys Ala Val Ile Val Ile Met Gly Asp Asp Pro Lys Glu
          100          105          110
Asp Leu Ala Val Leu Ala Lys Arg Leu Glu Asp Gln Gln Arg Ser Arg
          115          120          125
Asp Pro Gln Leu Gln Val Val Thr Asn Lys Ala Ile Glu Leu Lys Gly
          130          135          140
His Lys Met Gln Gln Leu Asp Ser Ile Ile Ser Ala Lys Gly Gln Thr
145           150           155           160
Ala Tyr Ser Ser Val Ile Leu Gly Asn Val Gly Asn Gln Leu Leu Thr
          165          170          175
Met Gln Ile Thr Leu Pro Ala Asp Asp Gln Gln Lys Ala Gln Thr Thr
          180          185          190
Ala Glu Asn Ile Ile Asn Thr Leu Val Ile Gln
          195          200

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&lt;210&gt; 245

&lt;211&gt; 324

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 245

```

Met Ala Asn Met Phe Ala Leu Ile Leu Val Ile Ala Thr Leu Val Thr
 1           5           10           15
Gly Ile Leu Trp Cys Val Asp Lys Phe Phe Phe Ala Pro Lys Arg Arg
          20           25           30
Glu Arg Gln Ala Ala Ala Gln Ala Ala Gly Asp Ser Leu Asp Lys
          35           40           45
Ala Thr Leu Lys Lys Val Ala Pro Lys Pro Gly Trp Leu Glu Thr Gly
          50           55           60
Ala Ser Val Phe Pro Val Leu Ala Ile Val Leu Ile Val Arg Ser Phe
65           70           75           80
Ile Tyr Glu Pro Phe Gln Ile Pro Ser Gly Ser Met Met Pro Thr Leu
          85           90           95
Leu Ile Gly Asp Phe Ile Leu Val Glu Lys Phe Ala Tyr Gly Ile Lys
          100          105          110
Asp Pro Ile Tyr Gln Lys Thr Leu Ile Glu Thr Gly His Pro Lys Arg
          115          120          125
Gly Asp Ile Val Val Phe Lys Tyr Pro Glu Asp Pro Lys Leu Asp Tyr
          130          135          140
Ile Lys Arg Ala Val Gly Leu Pro Gly Asp Lys Val Thr Tyr Asp Pro
145           150           155           160
Val Ser Lys Glu Leu Thr Ile Gln Pro Gly Cys Ser Ser Gly Gln Ala
          165          170          175
Cys Glu Asn Ala Leu Pro Val Thr Tyr Ser Asn Val Glu Pro Ser Asp
          180          185          190
Phe Val Gln Thr Phe Ser Arg Arg Asn Gly Gly Glu Ala Thr Ser Gly

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195	200	205
Phe Phe Glu Val Pro Lys Asn Glu Thr Lys Glu Asn Gly Ile Arg Leu		
210	215	220
Ser Glu Arg Lys Glu Thr Leu Gly Asp Val Thr His Arg Ile Leu Thr		
225	230	235
Val Pro Ile Ala Gln Asp Gln Val Gly Met Tyr Tyr Gln Gln Pro Gly		
245	250	255
Gln Gln Leu Ala Thr Trp Ile Val Pro Pro Gly Gln Tyr Phe Met Met		
260	265	270
Gly Asp Asn Arg Asp Asn Ser Ala Asp Ser Arg Tyr Trp Gly Phe Val		
275	280	285
Pro Glu Ala Asn Leu Val Gly Arg Ala Thr Ala Ile Trp Met Ser Phe		
290	295	300
Asp Lys Gln Glu Gly Glu Trp Pro Thr Gly Leu Arg Leu Ser Arg Ile		
305	310	315
Gly Gly Ile His		320

<210> 246  
 <211> 586  
 <212> PRT  
 <213> E. Coli

<400> 246

Met Thr Ile Thr Lys Leu Ala Trp Arg Asp Leu Val Pro Asp Thr Asp	
1 5 10 15	
Ser Tyr Gln Glu Ile Phe Ala Gln Pro His Leu Ile Asp Glu Asn Asp	
20 25 30	
Pro Leu Phe Ser Asp Thr Gln Pro Arg Leu Gln Phe Ala Leu Glu Gln	
35 40 45	
Leu Leu His Thr Arg Ala Ser Ser Ser Phe Met Leu Ala Lys Ala Pro	
50 55 60	
Glu Glu Ser Glu Tyr Leu Asn Leu Ile Ala Asn Ala Ala Arg Thr Leu	
65 70 75 80	
Gln Ser Asp Ala Gly Gln Leu Val Gly Gly His Tyr Glu Val Ser Gly	
85 90 95	
His Ser Ile Arg Leu Arg His Ala Val Ser Ala Asp Asp Asn Phe Ala	
100 105 110	
Thr Leu Thr Gln Val Val Ala Ala Asp Trp Val Glu Ala Glu Gln Leu	
115 120 125	
Phe Gly Cys Leu Arg Gln Phe Asn Gly Asp Ile Thr Leu Gln Pro Gly	
130 135 140	
Leu Val His Gln Ala Asn Gly Gly Ile Leu Ile Ser Leu Arg Thr	
145 150 155 160	
Leu Leu Ala Gln Pro Leu Leu Trp Met Arg Leu Lys Asn Ile Val Asn	
165 170 175	
Arg Glu Arg Phe Asp Trp Val Ala Phe Asp Glu Ser Arg Pro Leu Pro	
180 185 190	
Val Ser Val Pro Ser Met Pro Leu Lys Leu Lys Val Ile Leu Val Gly	
195 200 205	
Glu Arg Glu Ser Leu Ala Asp Phe Gln Glu Met Glu Pro Glu Leu Ser	
210 215 220	
Glu Gln Ala Ile Tyr Ser Glu Phe Glu Asp Thr Leu Gln Ile Val Asp	
225 230 235 240	
Ala Glu Ser Val Thr Gln Trp Cys Arg Trp Val Thr Phe Thr Ala Arg	
245 250 255	
His Asn His Leu Pro Ala Pro Gly Ala Asp Ala Trp Pro Ile Leu Ile	
260 265 270	
Arg Glu Ala Ala Arg Tyr Thr Gly Glu Gln Glu Thr Leu Pro Leu Ser	

275	280	285
Pro Gln Trp Ile Leu Arg Gln Cys Lys Glu Val Ala Ser Leu Cys Asp		
290	295	300
Gly Asp Thr Phe Ser Gly Glu Gln Leu Asn Leu Met Leu Gln Gln Arg		
305	310	315
Glu Trp Arg Glu Gly Phe Leu Ala Glu Arg Met Gln Asp Glu Ile Leu		
	325	330
Gln Glu Gln Ile Leu Ile Glu Thr Glu Gly Glu Arg Ile Gly Gln Ile		
	340	345
Asn Ala Leu Ser Val Ile Glu Phe Pro Gly His Pro Arg Ala Phe Gly		
	355	360
Glu Pro Ser Arg Ile Ser Cys Val Val His Ile Gly Asp Gly Glu Phe		
	370	375
Thr Asp Ile Glu Arg Lys Ala Glu Leu Gly Gly Asn Ile His Ala Lys		
	385	390
Gly Met Met Ile Met Gln Ala Phe Leu Met Ser Glu Leu Gln Leu Glu		
		405
Gln Gln Ile Pro Phe Ser Ala Ser Leu Thr Phe Glu Gln Ser Tyr Ser		
		420
Glu Val Asp Gly Asp Ser Ala Ser Met Ala Glu Leu Cys Ala Leu Ile		
		435
Ser Ala Leu Ala Asp Val Pro Val Asn Gln Ser Ile Ala Ile Thr Gly		
		450
Ser Val Asp Gln Phe Gly Arg Ala Gln Pro Val Gly Gly Leu Asn Glu		
		465
Lys Ile Glu Gly Phe Phe Ala Ile Cys Gln Gln Arg Glu Leu Thr Gly		
		485
Lys Gln Gly Val Ile Ile Pro Thr Ala Asn Val Arg His Leu Ser Leu		
		500
His Ser Glu Leu Val Lys Ala Val Glu Glu Gly Lys Phe Thr Ile Trp		
		515
Ala Val Asp Asp Val Thr Asp Ala Leu Pro Leu Leu Leu Asn Leu Val		
		530
Trp Asp Gly Glu Gly Gln Thr Thr Leu Met Gln Thr Ile Gln Glu Arg		
		545
Ile Ala Gln Ala Ser Gln Gln Glu Gly Arg His Arg Phe Pro Trp Pro		
		565
Leu Arg Trp Leu Asn Trp Phe Ile Pro Asn		
		580

&lt;210&gt; 247

&lt;211&gt; 394

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 247

Met Ser Lys Glu Lys Phe Glu Arg Thr Lys Pro His Val Asn Val Gly	
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Thr Ile Gly His Val Asp His Gly Lys Thr Thr Leu Thr Ala Ala Ile	
	20
Thr Thr Val Leu Ala Lys Thr Tyr Gly Gly Ala Ala Arg Ala Phe Asp	
	35
Gln Ile Asp Asn Ala Pro Glu Glu Lys Ala Arg Gly Ile Thr Ile Asn	
	50
Thr Ser His Val Glu Tyr Asp Thr Pro Thr Arg His Tyr Ala His Val	
	65
Asp Cys Pro Gly His Ala Asp Tyr Val Lys Asn Met Ile Thr Gly Ala	
	85
Ala Gln Met Asp Gly Ala Ile Leu Val Val Ala Ala Thr Asp Gly Pro	
	100

Met Pro Gln Thr Arg Glu His Ile Leu Leu Gly Arg Gln Val Gly Val  
 115 120 125  
 Pro Tyr Ile Ile Val Phe Leu Asn Lys Cys Asp Met Val Asp Asp Glu  
 130 135 140  
 Glu Leu Leu Glu Leu Val Glu Met Glu Val Arg Glu Leu Leu Ser Gln  
 145 150 155 160  
 Tyr Asp Phe Pro Gly Asp Asp Thr Pro Ile Val Arg Gly Ser Ala Leu  
 165 170 175  
 Lys Ala Leu Glu Gly Asp Ala Glu Trp Glu Ala Lys Ile Leu Glu Leu  
 180 185 190  
 Ala Gly Phe Leu Asp Ser Tyr Ile Pro Glu Pro Glu Arg Ala Ile Asp  
 195 200 205  
 Lys Pro Phe Leu Leu Pro Ile Glu Asp Val Phe Ser Ile Ser Gly Arg  
 210 215 220  
 Gly Thr Val Val Thr Gly Arg Val Glu Arg Gly Ile Ile Lys Val Gly  
 225 230 235 240  
 Glu Glu Val Glu Ile Val Gly Ile Lys Glu Thr Gln Lys Ser Thr Cys  
 245 250 255  
 Thr Gly Val Glu Met Phe Arg Lys Leu Leu Asp Glu Gly Arg Ala Gly  
 260 265 270  
 Glu Asn Val Gly Val Leu Leu Arg Gly Ile Lys Arg Glu Glu Ile Glu  
 275 280 285  
 Arg Gly Gln Val Leu Ala Lys Pro Gly Thr Ile Lys Pro His Thr Lys  
 290 295 300  
 Phe Glu Ser Glu Val Tyr Ile Leu Ser Lys Asp Glu Gly Gly Arg His  
 305 310 315 320  
 Thr Pro Phe Phe Lys Gly Tyr Arg Pro Gln Phe Tyr Phe Arg Thr Thr  
 325 330 335  
 Asp Val Thr Gly Thr Ile Glu Leu Pro Glu Gly Val Glu Met Val Met  
 340 345 350  
 Pro Gly Asp Asn Ile Lys Met Val Val Thr Leu Ile His Pro Ile Ala  
 355 360 365  
 Met Asp Asp Gly Leu Arg Phe Ala Ile Arg Glu Gly Gly Arg Thr Val  
 370 375 380  
 Gly Ala Gly Val Val Ala Lys Val Leu Gly  
 385 390

<210> 248  
 <211> 704  
 <212> PRT  
 <213> E. Coli

<400> 248  
 Met Ala Arg Thr Thr Pro Ile Ala Arg Tyr Arg Asn Ile Gly Ile Ser  
 1 5 10 15  
 Ala His Ile Asp Ala Gly Lys Thr Thr Thr Thr Glu Arg Ile Leu Phe  
 20 25 30  
 Tyr Thr Gly Val Asn His Lys Ile Gly Glu Val His Asp Gly Ala Ala  
 35 40 45  
 Thr Met Asp Trp Met Glu Gln Glu Glu Arg Gly Ile Thr Ile Thr  
 50 55 60  
 Ser Ala Ala Thr Thr Ala Phe Trp Ser Gly Met Ala Lys Gln Tyr Glu  
 65 70 75 80  
 Pro His Arg Ile Asn Ile Ile Asp Thr Pro Gly His Val Asp Phe Thr  
 85 90 95  
 Ile Glu Val Glu Arg Ser Met Arg Val Leu Asp Gly Ala Val Met Val  
 100 105 110  
 Tyr Cys Ala Val Gly Gly Val Gln Pro Gln Ser Glu Thr Val Trp Arg  
 115 120 125



Gln	Ala	Asn	Lys	Tyr	Lys	Val	Pro	Arg	Ile	Ala	Phe	Val	Asn	Lys	Met
130						135					140				
Asp	Arg	Met	Gly	Ala	Asn	Phe	Leu	Lys	Val	Val	Asn	Gln	Ile	Lys	Thr
145					150					155					160
Arg	Leu	Gly	Ala	Asn	Pro	Val	Pro	Leu	Gln	Leu	Ala	Ile	Gly	Ala	Glu
				165					170					175	
Glu	His	Phe	Thr	Gly	Val	Val	Asp	Leu	Val	Lys	Met	Lys	Ala	Ile	Asn
			180				185						190		
Trp	Asn	Asp	Ala	Asp	Gln	Gly	Val	Thr	Phe	Glu	Tyr	Glu	Asp	Ile	Pro
	195						200					205			
Ala	Asp	Met	Val	Glu	Leu	Ala	Asn	Glu	Trp	His	Gln	Asn	Leu	Ile	Glu
	210					215					220				
Ser	Ala	Ala	Glu	Ala	Ser	Glu	Glu	Leu	Met	Glu	Lys	Tyr	Leu	Gly	Gly
225					230					235					240
Glu	Glu	Leu	Thr	Glu	Ala	Glu	Ile	Lys	Gly	Ala	Leu	Arg	Gln	Arg	Val
				245					250					255	
Leu	Asn	Asn	Glu	Ile	Ile	Leu	Val	Thr	Cys	Gly	Ser	Ala	Phe	Lys	Asn
			260					265					270		
Lys	Gly	Val	Gln	Ala	Met	Leu	Asp	Ala	Val	Ile	Asp	Tyr	Leu	Pro	Ser
		275					280					285			
Pro	Val	Asp	Val	Pro	Ala	Ile	Asn	Gly	Ile	Leu	Asp	Asp	Gly	Lys	Asp
	290					295					300				
Thr	Pro	Ala	Glu	Arg	His	Ala	Ser	Asp	Asp	Glu	Pro	Phe	Ser	Ala	Leu
305					310					315					320
Ala	Phe	Lys	Ile	Ala	Thr	Asp	Pro	Phe	Val	Gly	Asn	Leu	Thr	Phe	Phe
				325					330					335	
Arg	Val	Tyr	Ser	Gly	Val	Val	Asn	Ser	Gly	Asp	Thr	Val	Leu	Asn	Ser
			340					345					350		
Val	Lys	Ala	Ala	Arg	Glu	Arg	Phe	Gly	Arg	Ile	Val	Gln	Met	His	Ala
		355					360					365			
Asn	Lys	Arg	Glu	Glu	Ile	Lys	Glu	Val	Arg	Ala	Gly	Asp	Ile	Ala	Ala
	370					375					380				
Ala	Ile	Gly	Leu	Lys	Asp	Val	Thr	Thr	Gly	Asp	Thr	Leu	Cys	Asp	Pro
385					390					395					400
Asp	Ala	Pro	Ile	Ile	Leu	Glu	Arg	Met	Glu	Phe	Pro	Glu	Pro	Val	Ile
				405					410					415	
Ser	Ile	Ala	Val	Glu	Pro	Lys	Thr	Lys	Ala	Asp	Gln	Glu	Lys	Met	Gly
			420					425					430		
Leu	Ala	Leu	Gly	Arg	Leu	Ala	Lys	Glu	Asp	Pro	Ser	Phe	Arg	Val	Trp
		435					440					445			
Thr	Asp	Glu	Glu	Ser	Asn	Gln	Thr	Ile	Ile	Ala	Gly	Met	Gly	Glu	Leu
	450					455					460				
His	Leu	Asp	Ile	Ile	Val	Asp	Arg	Met	Lys	Arg	Glu	Phe	Asn	Val	Glu
465					470					475					480
Ala	Asn	Val	Gly	Lys	Pro	Gln	Val	Ala	Tyr	Arg	Glu	Thr	Ile	Arg	Gln
				485					490					495	
Lys	Val	Thr	Asp	Val	Glu	Gly	Lys	His	Ala	Lys	Gln	Ser	Gly	Gly	Arg
			500					505					510		
Gly	Gln	Tyr	Gly	His	Val	Val	Ile	Asp	Met	Tyr	Pro	Leu	Glu	Pro	Gly
		515					520					525			
Ser	Asn	Pro	Lys	Gly	Tyr	Glu	Phe	Ile	Asn	Asp	Ile	Lys	Gly	Gly	Val
	530					535					540				
Ile	Pro	Gly	Glu	Tyr	Ile	Pro	Ala	Val	Asp	Lys	Gly	Ile	Gln	Glu	Gln
545					550					555					560
Leu	Lys	Ala	Gly	Pro	Leu	Ala	Gly	Tyr	Pro	Val	Val	Asp	Met	Gly	Ile
				565					570					575	
Arg	Leu	His	Phe	Gly	Ser	Tyr	His	Asp	Val	Asp	Ser	Ser	Glu	Leu	Ala
			580					585					590		
Phe	Lys	Leu	Ala	Ala	Ser	Ile	Ala	Phe	Lys	Glu	Gly	Phe	Lys	Lys	Ala
		595					600					605			
Lys	Pro	Val	Leu	Leu	Glu	Pro	Ile	Met	Lys	Val	Glu	Val	Glu	Thr	Pro

610	615	620
Glu Glu Asn Thr Gly Asp Val Ile Gly Asp Leu Ser Arg Arg Arg Gly		
625	630	635
Met Leu Lys Gly Gln Glu Ser Glu Val Thr Gly Val Lys Ile His Ala		640
	645	650
Glu Val Pro Leu Ser Glu Met Phe Gly Tyr Ala Thr Gln Leu Arg Ser		655
	660	665
Leu Thr Lys Gly Arg Ala Ser Tyr Thr Met Glu Phe Leu Lys Tyr Asp		670
	675	680
Glu Ala Pro Ser Asn Val Ala Gln Ala Val Ile Glu Ala Arg Gly Lys		685
	690	695
		700

<210> 249  
 <211> 179  
 <212> PRT  
 <213> E. Coli

<400> 249

Met Pro Arg Arg Val Ile Gly Gln Arg Lys Ile Leu Pro Asp Pro		
1	5	10
Lys Phe Gly Ser Glu Leu Leu Ala Lys Phe Val Asn Ile Leu Met Val		15
	20	25
Asp Gly Lys Lys Ser Thr Ala Glu Ser Ile Val Tyr Ser Ala Leu Glu		30
	35	40
Thr Leu Ala Gln Arg Ser Gly Lys Ser Glu Leu Glu Ala Phe Glu Val		45
	50	55
Ala Leu Glu Asn Val Arg Pro Thr Val Glu Val Lys Ser Arg Arg Val		60
	65	70
Gly Gly Ser Thr Tyr Gln Val Pro Val Glu Val Arg Pro Val Arg Arg		75
	85	90
Asn Ala Leu Ala Met Arg Trp Ile Val Glu Ala Ala Arg Lys Arg Gly		95
	100	105
Asp Lys Ser Met Ala Leu Arg Leu Ala Asn Glu Leu Ser Asp Ala Ala		110
	115	120
Glu Asn Lys Gly Thr Ala Val Lys Lys Arg Glu Asp Val His Arg Met		125
	130	135
Ala Glu Ala Asn Lys Ala Phe Ala His Tyr Arg Trp Leu Ser Leu Arg		140
	145	150
Ser Phe Ser His Gln Ala Gly Ala Ser Ser Lys Gln Pro Ala Leu Gly		155
	165	170
		175

Tyr Leu Asn

<210> 250  
 <211> 124  
 <212> PRT  
 <213> E. Coli

<400> 250

Met Ala Thr Val Asn Gln Leu Val Arg Lys Pro Arg Ala Arg Lys Val		
1	5	10
Ala Lys Ser Asn Val Pro Ala Leu Glu Ala Cys Pro Gln Lys Arg Gly		15
	20	25
Val Cys Thr Arg Val Tyr Thr Thr Pro Lys Lys Pro Asn Ser Ala		30
	35	40
Leu Arg Lys Val Cys Arg Val Arg Leu Thr Asn Gly Phe Glu Val Thr		45
	50	55
Ser Tyr Ile Gly Gly Glu Gly His Asn Leu Gln Glu His Ser Val Ile		60
	65	70
		75
		80

Leu Ile Arg Gly Gly Arg Val Lys Asp Leu Pro Gly Val Arg Tyr His  
                                     85                                    90                                    95  
 Thr Val Arg Gly Ala Leu Asp Cys Ser Gly Val Lys Asp Arg Lys Gln  
                                     100                                    105                                    110  
 Ala Arg Ser Lys Tyr Gly Val Lys Arg Pro Lys Ala  
                                     115                                    120

<210> 251  
 <211> 165  
 <212> PRT  
 <213> E. Coli

<400> 251  
 Met Ala Leu Asn Leu Gln Asp Lys Gln Ala Ile Val Ala Glu Val Ser  
   1                                    5                                    10                                    15  
 Glu Val Ala Lys Gly Ala Leu Ser Ala Val Val Ala Asp Ser Arg Gly  
                                     20                                    25                                    30  
 Val Thr Val Asp Lys Met Thr Glu Leu Arg Lys Ala Gly Arg Glu Ala  
                                     35                                    40                                    45  
 Gly Val Tyr Met Arg Val Val Arg Asn Thr Leu Leu Arg Arg Ala Val  
   50                                    55                                    60  
 Glu Gly Thr Pro Phe Glu Cys Leu Lys Asp Ala Phe Val Gly Pro Thr  
 65                                    70                                    75                                    80  
 Leu Ile Ala Tyr Ser Met Glu His Pro Gly Ala Ala Ala Arg Leu Phe  
                                     85                                    90                                    95  
 Lys Glu Phe Ala Lys Ala Asn Ala Lys Phe Glu Val Lys Ala Ala Ala  
                                     100                                    105                                    110  
 Phe Glu Gly Glu Leu Ile Pro Ala Ser Gln Ile Asp Arg Leu Ala Thr  
                                     115                                    120                                    125  
 Leu Pro Thr Tyr Glu Glu Ala Ile Ala Arg Leu Met Ala Thr Met Lys  
   130                                    135                                    140  
 Glu Ala Ser Ala Gly Lys Leu Val Arg Thr Leu Ala Ala Val Arg Asp  
 145                                    150                                    155                                    160  
 Ala Lys Glu Ala Ala  
                                     165

<210> 252  
 <211> 121  
 <212> PRT  
 <213> E. Coli

<400> 252  
 Met Ser Ile Thr Lys Asp Gln Ile Ile Glu Ala Val Ala Ala Met Ser  
   1                                    5                                    10                                    15  
 Val Met Asp Val Val Glu Leu Ile Ser Ala Met Glu Glu Lys Phe Gly  
                                     20                                    25                                    30  
 Val Ser Ala Ala Ala Ala Val Ala Val Ala Ala Gly Pro Val Glu Ala  
                                     35                                    40                                    45  
 Ala Glu Glu Lys Thr Glu Phe Asp Val Ile Leu Lys Ala Ala Gly Ala  
   50                                    55                                    60  
 Asn Lys Val Ala Val Ile Lys Ala Val Arg Gly Ala Thr Gly Leu Gly  
 65                                    70                                    75                                    80  
 Leu Lys Glu Ala Lys Asp Leu Val Glu Ser Ala Pro Ala Ala Leu Lys  
                                     85                                    90                                    95  
 Glu Gly Val Ser Lys Asp Asp Ala Glu Ala Leu Lys Lys Ala Leu Glu  
                                     100                                    105                                    110  
 Glu Ala Gly Ala Glu Val Glu Val Lys  
   115                                    120

<210> 253  
 <211> 714  
 <212> PRT  
 <213> E. Coli

<400> 253

Met	Ser	Arg	Ile	Ile	Met	Leu	Ile	Pro	Thr	Gly	Thr	Ser	Val	Gly	Leu
1				5					10					15	
Thr	Ser	Val	Ser	Leu	Gly	Val	Ile	Arg	Ala	Met	Glu	Arg	Lys	Gly	Val
			20					25					30		
Arg	Leu	Ser	Val	Phe	Lys	Pro	Ile	Ala	Gln	Pro	Arg	Thr	Gly	Gly	Asp
		35					40					45			
Ala	Pro	Asp	Gln	Thr	Thr	Thr	Ile	Val	Arg	Ala	Asn	Ser	Ser	Thr	Thr
	50					55					60				
Thr	Ala	Ala	Glu	Pro	Leu	Lys	Met	Ser	Tyr	Val	Glu	Gly	Leu	Leu	Ser
65					70					75				80	
Ser	Asn	Gln	Lys	Asp	Val	Leu	Met	Glu	Glu	Ile	Val	Ala	Asn	Tyr	His
			85						90					95	
Ala	Asn	Thr	Lys	Asp	Ala	Glu	Val	Val	Leu	Val	Glu	Gly	Leu	Val	Pro
			100					105						110	
Thr	Arg	Lys	His	Gln	Phe	Ala	Gln	Ser	Leu	Asn	Tyr	Glu	Ile	Ala	Lys
		115					120						125		
Thr	Leu	Asn	Ala	Glu	Ile	Val	Phe	Val	Met	Ser	Gln	Gly	Thr	Asp	Thr
	130					135						140			
Pro	Glu	Gln	Leu	Lys	Glu	Arg	Ile	Glu	Leu	Thr	Arg	Asn	Ser	Phe	Gly
145					150					155					160
Gly	Ala	Lys	Asn	Thr	Asn	Ile	Thr	Gly	Val	Ile	Val	Asn	Lys	Leu	Asn
			165						170					175	
Ala	Pro	Val	Asp	Glu	Gln	Gly	Arg	Thr	Arg	Pro	Asp	Leu	Ser	Glu	Ile
			180					185						190	
Phe	Asp	Asp	Ser	Ser	Lys	Ala	Lys	Val	Asn	Asn	Val	Asp	Pro	Ala	Lys
		195					200					205			
Leu	Gln	Glu	Ser	Ser	Pro	Leu	Pro	Val	Leu	Gly	Ala	Val	Pro	Trp	Ser
	210					215					220				
Phe	Asp	Leu	Ile	Ala	Thr	Arg	Ala	Ile	Asp	Met	Ala	Arg	His	Leu	Asn
225					230					235				240	
Ala	Thr	Ile	Ile	Asn	Glu	Gly	Asp	Ile	Asn	Thr	Arg	Arg	Val	Lys	Ser
			245						250					255	
Val	Thr	Phe	Cys	Ala	Arg	Ser	Ile	Pro	His	Met	Leu	Glu	His	Phe	Arg
			260					265					270		
Ala	Gly	Ser	Leu	Leu	Val	Thr	Ser	Ala	Asp	Arg	Pro	Asp	Val	Leu	Val
		275					280					285			
Ala	Ala	Cys	Leu	Ala	Ala	Met	Asn	Gly	Val	Glu	Ile	Gly	Ala	Leu	Leu
	290					295					300				
Leu	Thr	Gly	Gly	Tyr	Glu	Met	Asp	Ala	Arg	Ile	Ser	Lys	Leu	Cys	Glu
305					310					315				320	
Arg	Ala	Phe	Ala	Thr	Gly	Leu	Pro	Val	Phe	Met	Val	Asn	Thr	Asn	Thr
			325						330					335	
Trp	Gln	Thr	Ser	Leu	Ser	Leu	Gln	Ser	Phe	Asn	Leu	Glu	Val	Pro	Val
			340					345					350		
Asp	Asp	His	Glu	Arg	Ile	Glu	Lys	Val	Gln	Glu	Tyr	Val	Ala	Asn	Tyr
		355					360					365			
Ile	Asn	Ala	Asp	Trp	Ile	Glu	Ser	Leu	Thr	Ala	Thr	Ser	Glu	Arg	Ser
	370					375					380				
Arg	Arg	Leu	Ser	Pro	Pro	Ala	Phe	Arg	Tyr	Gln	Leu	Thr	Glu	Leu	Ala
385					390					395				400	
Arg	Lys	Ala	Gly	Lys	Arg	Ile	Val	Leu	Pro	Glu	Gly	Asp	Glu	Pro	Arg
			405						410					415	
Thr	Val	Lys	Ala	Ala	Ala	Ile	Cys	Ala	Glu	Arg	Gly	Ile	Ala	Thr	Cys
			420					425					430		

Val Leu Leu Gly Asn Pro Ala Glu Ile Asn Arg Val Ala Ala Ser Gln  
 435 440 445  
 Gly Val Glu Leu Gly Ala Gly Ile Glu Ile Val Asp Pro Glu Val Val  
 450 455 460  
 Arg Glu Ser Tyr Val Gly Arg Leu Val Glu Leu Arg Lys Asn Lys Gly  
 465 470 475 480  
 Met Thr Glu Thr Val Ala Arg Glu Gln Leu Glu Asp Asn Val Val Leu  
 485 490 495  
 Gly Thr Leu Met Leu Glu Gln Asp Glu Val Asp Gly Leu Val Ser Gly  
 500 505 510  
 Ala Val His Thr Thr Ala Asn Thr Ile Arg Pro Pro Leu Gln Leu Ile  
 515 520 525  
 Lys Thr Ala Pro Gly Ser Ser Leu Val Ser Ser Val Phe Phe Met Leu  
 530 535 540  
 Leu Pro Glu Gln Val Tyr Val Tyr Gly Asp Cys Ala Ile Asn Pro Asp  
 545 550 555 560  
 Pro Thr Ala Glu Gln Leu Ala Glu Ile Ala Ile Gln Ser Ala Asp Ser  
 565 570 575  
 Ala Ala Ala Phe Gly Ile Glu Pro Arg Val Ala Met Leu Ser Tyr Ser  
 580 585 590  
 Thr Gly Thr Ser Gly Ala Gly Ser Asp Val Glu Lys Val Arg Glu Ala  
 595 600 605  
 Thr Arg Leu Ala Gln Glu Lys Arg Pro Asp Leu Met Ile Asp Gly Pro  
 610 615 620  
 Leu Gln Tyr Asp Ala Ala Val Met Ala Asp Val Ala Lys Ser Lys Ala  
 625 630 635 640  
 Pro Asn Ser Pro Val Ala Gly Arg Ala Thr Val Phe Ile Phe Pro Asp  
 645 650 655  
 Leu Asn Thr Gly Asn Thr Thr Tyr Lys Ala Val Gln Arg Ser Ala Asp  
 660 665 670  
 Leu Ile Ser Ile Gly Pro Met Leu Gln Gly Met Arg Lys Pro Val Asn  
 675 680 685  
 Asp Leu Ser Arg Gly Ala Leu Val Asp Asp Ile Val Tyr Thr Ile Ala  
 690 695 700  
 Leu Thr Ala Ile Gln Ser Ala Gln Gln Gln  
 705 710

<210> 254  
 <211> 588  
 <212> PRT  
 <213> E. Coli

<400> 254  
 Met Asn Asn Ser Ile Asn His Lys Phe His His Ile Ser Arg Ala Glu  
 1 5 10 15  
 Tyr Gln Glu Leu Ala Val Ser Arg Gly Asp Ala Val Ala Asp Tyr  
 20 25 30  
 Ile Ile Asp Asn Val Ser Ile Leu Asp Leu Ile Asn Gly Gly Glu Ile  
 35 40 45  
 Ser Gly Pro Ile Val Ile Lys Gly Arg Tyr Ile Ala Gly Val Gly Ala  
 50 55 60  
 Glu Tyr Thr Asp Ala Pro Ala Leu Gln Arg Ile Asp Ala Arg Gly Ala  
 65 70 75 80  
 Thr Ala Val Pro Gly Phe Ile Asp Ala His Leu His Ile Glu Ser Ser  
 85 90 95  
 Met Met Thr Pro Val Thr Phe Glu Thr Ala Thr Leu Pro Arg Gly Leu  
 100 105 110  
 Thr Thr Val Ile Cys Asp Pro His Glu Ile Val Asn Val Met Gly Glu  
 115 120 125  
 Ala Gly Phe Ala Trp Phe Ala Arg Cys Ala Glu Gln Ala Arg Gln Asn

$\langle 210 \rangle$	255
$\langle 211 \rangle$	408

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 255

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Met Ala Tyr Cys Asn Pro Gly Leu Glu Ser Arg Pro Asn Lys Arg Asn
 1      5      10      15
Ala Leu Arg Arg His Val Val Thr Gly Ile Gly Met Lys Ile Val Ile
 20      25      30
Ala Pro Asp Ser Tyr Lys Glu Ser Leu Ser Ala Ser Glu Val Ala Gln
 35      40      45
Ala Ile Glu Lys Gly Phe Arg Glu Ile Phe Pro Asp Ala Gln Tyr Val
 50      55      60
Ser Val Pro Val Ala Asp Gly Gly Glu Gly Thr Val Glu Ala Met Ile
 65      70      75      80
Ala Ala Thr Gln Gly Ala Glu Arg His Ala Trp Val Thr Gly Pro Leu
 85      90      95
Gly Glu Lys Val Asn Ala Ser Trp Gly Ile Ser Gly Asp Gly Lys Thr
100      105      110
Ala Phe Ile Glu Met Ala Ala Ala Ser Gly Leu Glu Leu Val Pro Ala
115      120      125
Glu Lys Arg Asp Pro Leu Val Thr Thr Ser Arg Gly Thr Gly Glu Leu
130      135      140
Ile Leu Gln Ala Leu Glu Ser Gly Ala Thr Asn Ile Ile Ile Gly Ile
145      150      155      160
Gly Gly Ser Ala Thr Asn Asp Gly Gly Ala Gly Met Val Gln Ala Leu
165      170      175
Gly Ala Lys Leu Cys Asp Ala Asn Gly Asn Glu Ile Gly Phe Gly Gly
180      185      190
Gly Ser Leu Asn Thr Leu Asn Asp Ile Asp Ile Ser Gly Leu Asp Pro
195      200      205
Arg Leu Lys Asp Cys Val Ile Arg Val Ala Cys Asp Val Thr Asn Pro
210      215      220
Leu Val Gly Asp Asn Gly Ala Ser Arg Ile Phe Gly Pro Gln Lys Gly
225      230      235      240
Ala Ser Glu Ala Met Ile Val Glu Leu Asp Asn Asn Leu Ser His Tyr
245      250      255
Ala Glu Val Ile Lys Lys Ala Leu His Val Asp Val Lys Asp Val Pro
260      265      270
Gly Ala Gly Ala Ala Gly Gly Met Gly Ala Ala Leu Met Ala Phe Leu
275      280      285
Gly Ala Glu Leu Lys Ser Gly Ile Glu Ile Val Thr Thr Ala Leu Asn
290      295      300
Leu Glu Glu His Ile His Asp Cys Thr Leu Val Ile Thr Gly Glu Gly
305      310      315      320
Arg Ile Asp Ser Gln Ser Ile His Gly Lys Val Pro Ile Gly Val Ala
325      330      335
Asn Val Ala Lys Lys Tyr His Lys Pro Val Ile Gly Ile Ala Gly Ser
340      345      350
Leu Thr Asp Asp Val Gly Val Val His Gln His Gly Ile Asp Ala Val
355      360      365
Phe Ser Val Leu Thr Ser Ile Gly Thr Leu Asp Glu Ala Phe Arg Gly
370      375      380
Ala Tyr Asp Asn Ile Cys Arg Ala Ser Arg Asn Ile Ala Ala Thr Leu
385      390      395      400
Ala Ile Gly Met Arg Asn Ala Gly
405

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&lt;210&gt; 256

&lt;211&gt; 299

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 256

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Met Ile Asp Met Thr Met Lys Val Gly Phe Ile Gly Leu Gly Ile Met
 1           5           10           15
Gly Lys Pro Met Ser Lys Asn Leu Leu Lys Ala Gly Tyr Ser Leu Val
 20           25           30
Val Ala Asp Arg Asn Pro Glu Ala Ile Ala Asp Val Ile Ala Ala Gly
 35           40           45
Ala Glu Thr Ala Ser Thr Ala Lys Ala Ile Ala Glu Gln Cys Asp Val
 50           55           60
Ile Ile Thr Met Leu Pro Asn Ser Pro His Val Lys Glu Val Ala Leu
 65           70           75           80
Gly Glu Asn Gly Ile Ile Glu Gly Ala Lys Pro Gly Thr Val Leu Ile
 85           90           95
Asp Met Ser Ser Ile Ala Pro Leu Ala Ser Arg Glu Ile Ser Glu Ala
 100          105          110
Leu Lys Ala Lys Gly Ile Asp Met Leu Asp Ala Pro Val Ser Gly Gly
 115          120          125
Glu Pro Lys Ala Ile Asp Gly Thr Leu Ser Val Met Val Gly Gly Asp
 130          135          140
Lys Ala Ile Phe Asp Lys Tyr Tyr Asp Leu Met Lys Ala Met Ala Gly
 145          150          155          160
Ser Val Val His Thr Gly Glu Ile Gly Ala Gly Asn Val Thr Lys Leu
 165          170          175
Ala Asn Gln Val Ile Val Ala Leu Asn Ile Ala Ala Met Ser Glu Ala
 180          185          190
Leu Thr Leu Ala Thr Lys Ala Gly Val Asn Pro Asp Leu Val Tyr Gln
 195          200          205
Ala Ile Arg Gly Gly Leu Ala Gly Ser Thr Val Leu Asp Ala Lys Ala
 210          215          220
Pro Met Val Met Asp Arg Asn Phe Lys Pro Gly Phe Arg Ile Asp Leu
 225          230          235          240
His Ile Lys Asp Leu Ala Asn Ala Leu Asp Thr Ser His Gly Val Gly
 245          250          255
Ala Gln Leu Pro Leu Thr Ala Ala Val Met Glu Met Met Gln Ala Leu
 260          265          270
Arg Ala Asp Gly Leu Gly Thr Ala Asp His Ser Ala Leu Ala Cys Tyr
 275          280          285
Tyr Glu Lys Leu Ala Lys Val Glu Val Thr Arg
 290          295

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&lt;210&gt; 257

&lt;211&gt; 256

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 257

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Met Asn Asn Asp Val Phe Pro Asn Lys Phe Lys Ala Ala Leu Ala Ala
 1           5           10           15
Lys Gln Val Gln Ile Gly Cys Trp Ser Ala Leu Ser Asn Pro Ile Ser
 20           25           30
Thr Glu Val Leu Gly Leu Ala Gly Phe Asp Trp Leu Val Leu Asp Gly
 35           40           45
Glu His Ala Pro Asn Asp Ile Ser Thr Phe Ile Pro Gln Leu Met Ala
 50           55           60
Leu Lys Gly Ser Ala Ser Ala Pro Val Val Arg Val Pro Thr Asn Glu
 65           70           75           80
Pro Val Ile Ile Lys Arg Leu Leu Asp Ile Gly Phe Tyr Asn Phe Leu

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Ile	Pro	Phe	Val	Glu	Thr	Lys	Glu	Glu	Ala	Glu	Leu	Ala	Val	Ala	Ser
			100					105					110		
Thr	Arg	Tyr	Pro	Pro	Glu	Gly	Ile	Arg	Gly	Val	Ser	Val	Ser	His	Arg
		115					120						125		
Ala	Asn	Met	Phe	Gly	Thr	Val	Ala	Asp	Tyr	Phe	Ala	Gln	Ser	Asn	Lys
	130					135					140				
Asn	Ile	Thr	Ile	Leu	Val	Gln	Ile	Glu	Ser	Gln	Gln	Gly	Val	Asp	Asn
145				150					155					160	
Val	Asp	Ala	Ile	Ala	Ala	Thr	Glu	Gly	Val	Asp	Gly	Ile	Phe	Val	Gly
			165					170						175	
Pro	Ser	Asp	Leu	Ala	Ala	Ala	Leu	Gly	His	Leu	Gly	Asn	Ala	Ser	His
		180					185						190		
Pro	Asp	Val	Gln	Lys	Ala	Ile	Gln	His	Ile	Phe	Asn	Arg	Ala	Ser	Ala
	195						200					205			
His	Gly	Lys	Pro	Ser	Gly	Ile	Leu	Ala	Pro	Val	Glu	Ala	Asp	Ala	Arg
	210					215					220				
Arg	Tyr	Leu	Glu	Trp	Gly	Ala	Thr	Phe	Val	Ala	Val	Gly	Ser	Asp	Leu
225					230					235					240
Gly	Val	Phe	Arg	Ser	Ala	Thr	Gln	Lys	Leu	Ala	Asp	Thr	Phe	Lys	Lys
			245						250					255	

&lt;210&gt; 258

&lt;211&gt; 444

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 258

Met	Ile	Leu	Asp	Thr	Val	Asp	Glu	Lys	Lys	Lys	Gly	Val	His	Thr	Arg
1				5					10					15	
Tyr	Leu	Ile	Leu	Leu	Ile	Ile	Phe	Ile	Val	Thr	Ala	Val	Asn	Tyr	Ala
			20				25						30		
Asp	Arg	Ala	Thr	Leu	Ser	Ile	Ala	Gly	Thr	Glu	Val	Ala	Lys	Glu	Leu
	35						40					45			
Gln	Leu	Ser	Ala	Val	Ser	Met	Gly	Tyr	Ile	Phe	Ser	Ala	Phe	Gly	Trp
	50					55					60				
Ala	Tyr	Leu	Leu	Met	Gln	Ile	Pro	Gly	Gly	Trp	Leu	Leu	Asp	Lys	Phe
65				70						75				80	
Gly	Ser	Lys	Lys	Val	Tyr	Thr	Tyr	Ser	Leu	Phe	Phe	Trp	Ser	Leu	Phe
			85						90					95	
Thr	Phe	Leu	Gln	Gly	Phe	Val	Asp	Met	Phe	Pro	Leu	Ala	Trp	Ala	Gly
			100				105						110		
Ile	Ser	Met	Phe	Phe	Met	Arg	Phe	Met	Leu	Gly	Phe	Ser	Glu	Ala	Pro
	115						120					125			
Ser	Phe	Pro	Ala	Asn	Ala	Arg	Ile	Val	Ala	Ala	Trp	Phe	Pro	Thr	Lys
	130					135					140				
Glu	Arg	Gly	Thr	Ala	Ser	Ala	Ile	Phe	Asn	Ser	Ala	Gln	Tyr	Phe	Ser
145					150					155				160	
Leu	Ala	Leu	Phe	Ser	Pro	Leu	Leu	Gly	Trp	Leu	Thr	Phe	Ala	Trp	Gly
			165					170						175	
Trp	Glu	His	Val	Phe	Thr	Val	Met	Gly	Val	Ile	Gly	Phe	Val	Leu	Thr
			180					185					190		
Ala	Leu	Trp	Ile	Lys	Leu	Ile	His	Asn	Pro	Thr	Asp	His	Pro	Arg	Met
	195						200					205			
Ser	Ala	Glu	Glu	Leu	Lys	Phe	Ile	Ser	Glu	Asn	Gly	Ala	Val	Val	Asp
	210					215					220				
Met	Asp	His	Lys	Lys	Pro	Gly	Ser	Ala	Ala	Ala	Ser	Gly	Pro	Lys	Leu
225					230					235					240
His	Tyr	Ile	Lys	Gln	Leu	Leu	Ser	Asn	Arg	Met	Met	Leu	Gly	Val	Phe
				245					250					255	

Phe Gly Gln Tyr Phe Ile Asn Thr Ile Thr Trp Phe Phe Leu Thr Trp  
 260 265 270  
 Phe Pro Ile Tyr Leu Val Gln Glu Lys Gly Met Ser Ile Leu Lys Val  
 275 280 285  
 Gly Leu Val Ala Ser Ile Pro Ala Leu Cys Gly Phe Ala Gly Gly Val  
 290 295 300  
 Leu Gly Gly Val Phe Ser Asp Tyr Leu Ile Lys Arg Gly Leu Ser Leu  
 305 310 315 320  
 Thr Leu Ala Arg Lys Leu Pro Ile Val Leu Gly Met Leu Leu Ala Ser  
 325 330 335  
 Thr Ile Ile Leu Cys Asn Tyr Thr Asn Asn Thr Thr Leu Val Val Met  
 340 345 350  
 Leu Met Ala Leu Ala Phe Phe Gly Lys Gly Phe Gly Ala Leu Gly Trp  
 355 360 365  
 Pro Val Ile Ser Asp Thr Ala Pro Lys Glu Ile Val Gly Leu Cys Gly  
 370 375 380  
 Gly Val Phe Asn Val Phe Gly Asn Val Ala Ser Ile Val Thr Pro Leu  
 385 390 395 400  
 Val Ile Gly Tyr Leu Val Ser Glu Leu His Ser Phe Asn Ala Ala Leu  
 405 410 415  
 Val Phe Val Gly Cys Ser Ala Leu Met Ala Met Val Cys Tyr Leu Phe  
 420 425 430  
 Val Val Gly Asp Ile Lys Arg Met Glu Leu Gln Lys  
 435 440

&lt;210&gt; 259

&lt;211&gt; 511

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 259

Met Gln Thr Ser Asp Thr Arg Ala Leu Pro Leu Leu Cys Ala Arg Ser  
 1 5 10 15  
 Val Tyr Lys Gln Tyr Ser Gly Val Asn Val Leu Lys Gly Ile Asp Phe  
 20 25 30  
 Thr Leu His Gln Gly Glu Val His Ala Leu Leu Gly Gly Asn Gly Ala  
 35 40 45  
 Gly Lys Ser Thr Leu Met Lys Ile Ile Ala Gly Ile Thr Pro Ala Asp  
 50 55 60  
 Ser Gly Thr Leu Glu Ile Glu Gly Asn Asn Tyr Val Arg Leu Thr Pro  
 65 70 75 80  
 Val His Ala His Gln Leu Gly Ile Tyr Leu Val Pro Gln Glu Pro Leu  
 85 90 95  
 Leu Phe Pro Ser Leu Ser Ile Lys Glu Asn Ile Leu Phe Gly Leu Ala  
 100 105 110  
 Lys Lys Gln Leu Ser Met Gln Lys Met Lys Asn Leu Leu Ala Ala Leu  
 115 120 125  
 Gly Cys Gln Phe Asp Leu His Ser Leu Ala Gly Ser Leu Asp Val Ala  
 130 135 140  
 Asp Arg Gln Met Val Glu Ile Leu Arg Gly Leu Met Arg Asp Ser Arg  
 145 150 155 160  
 Ile Leu Ile Leu Asp Glu Pro Thr Ala Ser Leu Thr Pro Ala Glu Thr  
 165 170 175  
 Glu Arg Leu Phe Ser Arg Leu Gln Glu Leu Leu Ala Thr Gly Val Gly  
 180 185 190  
 Ile Val Phe Ile Ser His Lys Leu Pro Glu Ile Arg Gln Ile Ala Asp  
 195 200 205  
 Arg Ile Ser Val Met Arg Asp Gly Thr Ile Ala Leu Ser Gly Lys Thr  
 210 215 220  
 Ser Glu Leu Ser Thr Asp Asp Ile Ile Gln Ala Ile Thr Pro Ala Val

225	Arg	Glu	Lys	Ser	Leu	Ser	Ala	Ser	Gln	Lys	Leu	Trp	Leu	Glu	Leu	Pro
					245					250					255	
	Gly	Asn	Arg	Pro	Gln	His	Ala	Ala	Gly	Thr	Pro	Val	Leu	Thr	Leu	Glu
				260					265					270		
	Asn	Leu	Thr	Gly	Glu	Gly	Phe	Arg	Asn	Val	Ser	Leu	Thr	Leu	Asn	Ala
			275					280					285			
	Gly	Glu	Ile	Leu	Gly	Leu	Ala	Gly	Leu	Val	Gly	Ala	Gly	Arg	Thr	Glu
		290					295				300					
	Leu	Ala	Glu	Thr	Leu	Tyr	Gly	Leu	Arg	Thr	Leu	Arg	Gly	Gly	Arg	Ile
305						310					315				320	
	Met	Leu	Asn	Gly	Lys	Glu	Ile	Asn	Lys	Leu	Ser	Thr	Gly	Glu	Arg	Leu
				325						330					335	
	Leu	Arg	Gly	Leu	Val	Tyr	Leu	Pro	Glu	Asp	Arg	Gln	Ser	Ser	Gly	Leu
			340						345					350		
	Asn	Leu	Asp	Ala	Ser	Leu	Ala	Trp	Asn	Val	Cys	Ala	Leu	Thr	His	Asn
		355					360						365			
	Leu	Arg	Gly	Phe	Trp	Ala	Lys	Thr	Ala	Lys	Asp	Asn	Ala	Thr	Leu	Glu
		370					375					380				
	Arg	Tyr	Arg	Arg	Ala	Leu	Asn	Ile	Lys	Phe	Asn	Gln	Pro	Glu	Gln	Ala
385						390					395				400	
	Ala	Arg	Thr	Leu	Ser	Gly	Gly	Asn	Gln	Gln	Lys	Ile	Leu	Ile	Ala	Lys
				405					410						415	
	Cys	Leu	Glu	Ala	Ser	Pro	Gln	Val	Leu	Ile	Val	Asp	Glu	Pro	Thr	Arg
			420				425						430			
	Gly	Val	Asp	Val	Ser	Ala	Arg	Asn	Asp	Ile	Tyr	Gln	Leu	Leu	Arg	Ser
		435					440					445				
	Ile	Ala	Ala	Gln	Asn	Val	Ala	Val	Leu	Leu	Ile	Ser	Ser	Asp	Leu	Glu
		450				455					460					
	Glu	Ile	Glu	Leu	Met	Ala	Asp	Arg	Val	Tyr	Val	Met	His	Gln	Gly	Glu
465					470					475					480	
	Ile	Thr	His	Ser	Ala	Leu	Thr	Glu	Arg	Asp	Ile	Asn	Val	Glu	Thr	Ile
				485					490					495		
	Met	Arg	Val	Ala	Phe	Gly	Asp	Ser	Gln	Arg	Gln	Glu	Ala	Ser	Cys	
			500					505					510			

&lt;210&gt; 260

&lt;211&gt; 342

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 260

Met	Leu	Lys	Phe	Ile	Gln	Asn	Asn	Arg	Glu	Ile	Thr	Ala	Leu	Leu	Ala
1				5					10					15	
Val	Val	Leu	Leu	Phe	Val	Leu	Pro	Gly	Phe	Leu	Asp	Arg	Gln	Tyr	Leu
			20					25					30		
Ser	Val	Gln	Thr	Leu	Thr	Met	Val	Tyr	Ser	Ser	Ala	Gln	Ile	Leu	Ile
		35				40						45			
Leu	Leu	Ala	Met	Gly	Ala	Thr	Leu	Val	Met	Leu	Thr	Arg	Asn	Ile	Asp
	50				55					60					
Val	Ser	Val	Gly	Ser	Ile	Thr	Gly	Met	Cys	Ala	Val	Leu	Leu	Gly	Met
65				70					75					80	
Leu	Leu	Asn	Ala	Gly	Tyr	Ser	Leu	Pro	Val	Ala	Cys	Val	Ala	Thr	Leu
			85					90					95		
Leu	Leu	Gly	Leu	Leu	Ala	Gly	Phe	Phe	Asn	Gly	Val	Leu	Val	Ala	Trp
		100					105					110			
Leu	Lys	Ile	Pro	Ala	Ile	Val	Ala	Thr	Leu	Gly	Thr	Leu	Gly	Leu	Tyr
	115				120						125				
Arg	Gly	Ile	Met	Leu	Leu	Trp	Thr	Gly	Gly	Lys	Trp	Ile	Glu	Gly	Leu
	130				135						140				

Pro Ala Glu Leu Lys Gln Leu Ser Ala Pro Leu Leu Leu Gly Val Ser  
 145 150 155 160  
 Ala Ile Gly Trp Leu Thr Ile Ile Leu Val Ala Phe Met Ala Trp Leu  
 165 170 175  
 Leu Ala Lys Thr Ala Phe Gly Arg Ser Phe Tyr Ala Thr Gly Asp Asn  
 180 185 190  
 Leu Gln Gly Ala Arg Gln Leu Gly Val Arg Thr Glu Ala Ile Arg Ile  
 195 200 205  
 Val Ala Phe Ser Leu Asn Gly Cys Met Ala Ala Leu Ala Gly Ile Val  
 210 215 220  
 Phe Ala Ser Gln Ile Gly Phe Ile Pro Asn Gln Thr Gly Thr Gly Leu  
 225 230 235 240  
 Glu Met Lys Ala Ile Ala Ala Cys Val Leu Gly Gly Ile Ser Leu Leu  
 245 250 255  
 Gly Gly Ser Gly Ala Ile Ile Gly Ala Val Leu Gly Ala Trp Phe Leu  
 260 265 270  
 Thr Gln Ile Asp Ser Val Leu Val Leu Leu Arg Ile Pro Ala Trp Trp  
 275 280 285  
 Asn Asp Phe Ile Ala Gly Leu Val Leu Leu Ala Val Leu Val Phe Asp  
 290 295 300  
 Gly Arg Leu Arg Cys Ala Leu Glu Arg Asn Leu Arg Arg Gln Lys Tyr  
 305 310 315 320  
 Ala Arg Phe Met Thr Pro Pro Pro Ser Val Lys Pro Ala Ser Ser Gly  
 325 330 335  
 Lys Lys Arg Glu Ala Ala  
 340

<210> 261  
 <211> 330  
 <212> PRT  
 <213> E. Coli

<400> 261  
 Met Arg Ile Arg Tyr Gly Trp Glu Leu Ala Leu Ala Ala Leu Leu Val  
 1 5 10 15  
 Ile Glu Ile Val Ala Phe Gly Ala Ile Asn Pro Arg Met Leu Asp Leu  
 20 25 30  
 Asn Met Leu Leu Phe Ser Thr Ser Asp Phe Ile Cys Ile Gly Ile Val  
 35 40 45  
 Ala Leu Pro Leu Thr Met Val Ile Val Ser Gly Gly Ile Asp Ile Ser  
 50 55 60  
 Phe Gly Ser Thr Ile Gly Leu Cys Ala Ile Ala Leu Gly Val Leu Phe  
 65 70 75 80  
 Gln Ser Gly Val Pro Met Pro Leu Ala Ile Leu Leu Thr Leu Leu Leu  
 85 90 95  
 Gly Ala Leu Cys Gly Leu Ile Asn Ala Gly Leu Ile Ile Tyr Thr Lys  
 100 105 110  
 Val Asn Pro Leu Val Ile Thr Leu Gly Thr Leu Tyr Leu Phe Ala Gly  
 115 120 125  
 Ser Ala Leu Leu Leu Ser Gly Met Ala Gly Ala Thr Gly Tyr Glu Gly  
 130 135 140  
 Ile Gly Gly Phe Pro Met Ala Phe Thr Asp Phe Ala Asn Leu Asp Val  
 145 150 155 160  
 Leu Gly Leu Pro Val Pro Leu Ile Ile Phe Leu Ile Cys Leu Leu Val  
 165 170 175  
 Phe Trp Leu Trp Leu His Lys Thr His Ala Gly Arg Asn Val Phe Leu  
 180 185 190  
 Ile Gly Gln Ser Pro Arg Val Ala Leu Tyr Ser Ala Ile Pro Val Asn  
 195 200 205  
 Arg Thr Leu Cys Ala Leu Tyr Ala Met Thr Gly Leu Ala Ser Ala Val  
 210 215 220

Ala Ala Val Leu Leu Val Ser Tyr Phe Gly Ser Ala Arg Ser Asp Leu  
 225 230 235 240  
 Gly Ala Ser Phe Leu Met Pro Ala Ile Thr Ala Val Val Leu Gly Gly  
 245 250 255  
 Ala Asn Ile Tyr Gly Gly Ser Gly Ser Ile Ile Gly Thr Ala Ile Ala  
 260 265 270  
 Val Leu Leu Val Gly Tyr Leu Gln Gly Leu Gln Met Ala Gly Val  
 275 280 285  
 Pro Asn Gln Val Ser Ser Ala Leu Ser Gly Ala Leu Ile Val Val  
 290 295 300  
 Val Val Gly Arg Ser Val Ser Leu His Arg Gln Gln Ile Lys Glu Trp  
 305 310 315 320  
 Leu Ala Arg Arg Ala Asn Asn Pro Leu Pro  
 325 330

<210> 262  
 <211> 340  
 <212> PRT  
 <213> E. Coli

<400> 262  
 Met Thr Leu His Arg Phe Lys Lys Ile Ala Leu Leu Ser Ala Leu Gly  
 1 5 10 15  
 Ile Ala Ala Ile Ser Met Asn Val Gln Ala Ala Glu Arg Ile Ala Phe  
 20 25 30  
 Ile Pro Lys Leu Val Gly Val Gly Phe Phe Thr Ser Gly Gly Asn Gly  
 35 40 45  
 Ala Gln Gln Ala Gly Lys Glu Leu Gly Val Asp Val Thr Tyr Asp Gly  
 50 55 60  
 Pro Thr Glu Pro Ser Val Ser Gly Gln Val Gln Leu Ile Asn Asn Phe  
 65 70 75 80  
 Val Asn Gln Gly Tyr Asn Ala Ile Ile Val Ser Ala Val Ser Pro Asp  
 85 90 95  
 Gly Leu Cys Pro Ala Leu Lys Arg Ala Met Gln Arg Gly Val Arg Val  
 100 105 110  
 Leu Thr Trp Asp Ser Asp Thr Lys Pro Glu Cys Arg Ser Tyr Tyr Ile  
 115 120 125  
 Asn Gln Gly Thr Pro Ala Gln Leu Gly Gly Met Leu Val Asp Met Ala  
 130 135 140  
 Ala Arg Gln Val Asn Lys Asp Lys Ala Lys Val Ala Phe Phe Tyr Ser  
 145 150 155 160  
 Ser Pro Thr Val Thr Asp Gln Asn Gln Trp Val Lys Glu Ala Lys Ala  
 165 170 175  
 Lys Ile Ala Lys Glu His Pro Gly Trp Glu Ile Val Thr Thr Gln Phe  
 180 185 190  
 Gly Tyr Asn Asp Ala Thr Lys Ser Leu Gln Thr Ala Glu Gly Ile Leu  
 195 200 205  
 Lys Ala Tyr Ser Asp Leu Asp Ala Ile Ile Ala Pro Asp Ala Asn Ala  
 210 215 220  
 Leu Pro Ala Ala Ala Gln Ala Ala Glu Asn Leu Lys Asn Asp Lys Val  
 225 230 235 240  
 Ala Ile Val Gly Phe Ser Thr Pro Asn Val Met Arg Pro Tyr Val Glu  
 245 250 255  
 Arg Gly Thr Val Lys Glu Phe Gly Leu Trp Asp Val Val Gln Gln Gly  
 260 265 270  
 Lys Ile Ser Val Tyr Val Ala Asp Ala Leu Leu Lys Lys Gly Ser Met  
 275 280 285  
 Lys Thr Gly Asp Lys Leu Asp Ile Lys Gly Val Gly Gln Val Glu Val

290	295	300
Ser Pro Asn Ser Val	Gln Gly Tyr Asp Tyr	Glu Ala Asp Gly Asn Gly
305	310	315
Ile Val Leu Leu Pro	Glu Arg Val Ile Phe	Asn Lys Glu Asn Ile Gly
	325	330
Lys Tyr Asp Phe		335
	340	

<210> 263  
 <211> 291  
 <212> PRT  
 <213> E. Coli

<400> 263

Met Ala Asp Leu Asp Asp Ile Lys Asp Gly Lys Asp Phe Arg Thr Asp	
1 5 10 15	
Gln Pro Gln Lys Asn Ile Pro Phe Thr Leu Lys Gly Cys Gly Ala Leu	
20 25 30	
Asp Trp Gly Met Gln Ser Arg Leu Ser Arg Ile Phe Asn Pro Lys Thr	
35 40 45	
Gly Lys Thr Val Met Leu Ala Phe Asp His Gly Tyr Phe Gln Gly Pro	
50 55 60	
Thr Thr Gly Leu Glu Arg Ile Asp Ile Asn Ile Ala Pro Leu Phe Glu	
65 70 75 80	
His Ala Asp Val Leu Met Cys Thr Arg Gly Ile Leu Arg Ser Val Val	
85 90 95	
Pro Pro Ala Thr Asn Arg Pro Val Val Leu Arg Ala Ser Gly Ala Asn	
100 105 110	
Ser Ile Leu Ala Glu Leu Ser Asn Glu Ala Val Ala Leu Ser Met Asp	
115 120 125	
Asp Ala Val Arg Leu Asn Ser Cys Ala Val Ala Ala Gln Val Tyr Ile	
130 135 140	
Gly Ser Glu Tyr Glu His Gln Ser Ile Lys Asn Ile Ile Gln Leu Val	
145 150 155 160	
Asp Ala Gly Met Lys Val Gly Met Pro Thr Met Ala Val Thr Gly Val	
165 170 175	
Gly Lys Asp Met Val Arg Asp Gln Arg Tyr Phe Ser Leu Ala Thr Arg	
180 185 190	
Ile Ala Ala Glu Met Gly Ala Gln Ile Ile Lys Thr Tyr Tyr Val Glu	
195 200 205	
Lys Gly Phe Glu Arg Ile Val Ala Gly Cys Pro Val Pro Ile Val Ile	
210 215 220	
Ala Gly Gly Lys Lys Leu Pro Glu Arg Glu Ala Leu Glu Met Cys Trp	
225 230 235 240	
Gln Ala Ile Asp Gln Gly Ala Ser Gly Val Asp Met Gly Arg Asn Ile	
245 250 255	
Phe Gln Ser Asp His Pro Val Ala Met Met Lys Ala Val Gln Ala Val	
260 265 270	
Val His His Asn Glu Thr Ala Asp Arg Ala Tyr Glu Leu Tyr Leu Ser	
275 280 285	
Glu Lys Gln	
290	

<210> 264  
 <211> 96  
 <212> PRT  
 <213> E. Coli

<400> 264

Met His Val Thr Leu Val Glu Ile Asn Val His Glu Asp Lys Val Asp  
 1 5 10 15  
 Glu Phe Ile Glu Val Phe Arg Gln Asn His Leu Gly Ser Val Gln Glu  
 20 25 30  
 Glu Gly Asn Leu Arg Phe Asp Val Leu Gln Asp Pro Glu Val Asn Ser  
 35 40 45  
 Arg Phe Tyr Ile Tyr Glu Ala Tyr Lys Asp Glu Asp Ala Val Ala Phe  
 50 55 60  
 His Lys Thr Thr Pro His Tyr Lys Thr Cys Val Ala Lys Leu Glu Ser  
 65 70 75 80  
 Leu Met Thr Gly Pro Arg Lys Lys Arg Leu Phe Asn Gly Leu Met Pro  
 85 90 95

<210> 265  
 <211> 383  
 <212> PRT  
 <213> E. Coli

<400> 265

Met Phe Glu Pro Met Glu Leu Thr Asn Asp Ala Val Ile Lys Val Ile  
 1 5 10 15  
 Gly Val Gly Gly Gly Gly Asn Ala Val Glu His Met Val Arg Glu  
 20 25 30  
 Arg Ile Glu Gly Val Glu Phe Phe Ala Val Asn Thr Asp Ala Gln Ala  
 35 40 45  
 Leu Arg Lys Thr Ala Val Gly Gln Thr Ile Gln Ile Gly Ser Gly Ile  
 50 55 60  
 Thr Lys Gly Leu Gly Ala Gly Ala Asn Pro Glu Val Gly Arg Asn Ala  
 65 70 75 80  
 Ala Asp Glu Asp Arg Asp Ala Leu Arg Ala Ala Leu Glu Gly Ala Asp  
 85 90 95  
 Met Val Phe Ile Ala Ala Gly Met Gly Gly Thr Gly Thr Gly Ala  
 100 105 110  
 Ala Pro Val Val Ala Glu Val Ala Lys Asp Leu Gly Ile Leu Thr Val  
 115 120 125  
 Ala Val Val Thr Lys Pro Phe Asn Phe Glu Gly Lys Lys Arg Met Ala  
 130 135 140  
 Phe Ala Glu Gln Gly Ile Thr Glu Leu Ser Lys His Val Asp Ser Leu  
 145 150 155 160  
 Ile Thr Ile Pro Asn Asp Lys Leu Leu Lys Val Leu Gly Arg Gly Ile  
 165 170 175  
 Ser Leu Leu Asp Ala Phe Gly Ala Ala Asn Asp Val Leu Lys Gly Ala  
 180 185 190  
 Val Gln Gly Ile Ala Glu Leu Ile Thr Arg Pro Gly Leu Met Asn Val  
 195 200 205  
 Asp Phe Ala Asp Val Arg Thr Val Met Ser Glu Met Gly Tyr Ala Met  
 210 215 220  
 Met Gly Ser Gly Val Ala Ser Gly Glu Asp Arg Ala Glu Glu Ala Ala  
 225 230 235 240  
 Glu Met Ala Ile Ser Ser Pro Leu Leu Glu Asp Ile Asp Leu Ser Gly  
 245 250 255  
 Ala Arg Gly Val Leu Val Asn Ile Thr Ala Gly Phe Asp Leu Arg Leu  
 260 265 270  
 Asp Glu Phe Glu Thr Val Gly Asn Thr Ile Arg Ala Phe Ala Ser Asp  
 275 280 285  
 Asn Ala Thr Val Val Ile Gly Thr Ser Leu Asp Pro Asp Met Asn Asp  
 290 295 300  
 Glu Leu Arg Val Thr Val Val Ala Thr Gly Ile Gly Met Asp Lys Arg  
 305 310 315 320  
 Pro Glu Ile Thr Leu Val Thr Asn Lys Gln Val Gln Gln Pro Val Met

325 330 335  
 Asp Arg Tyr Gln Gln His Gly Met Ala Pro Leu Thr Gln Glu Gln Lys  
 340 345 350  
 Pro Val Ala Lys Val Val Asn Asp Asn Ala Pro Gln Thr Ala Lys Glu  
 355 360 365  
 Pro Asp Tyr Leu Asp Ile Pro Ala Phe Leu Arg Lys Gln Ala Asp  
 370 375 380

<210> 266  
 <211> 1014  
 <212> PRT  
 <213> E. Coli

<400> 266  
 Met Asp Val Ser Arg Arg Gln Phe Phe Lys Ile Cys Ala Gly Gly Met  
 1 5 10 15  
 Ala Gly Thr Thr Val Ala Ala Leu Gly Phe Ala Pro Lys Gln Ala Leu  
 20 25 30  
 Ala Gln Ala Arg Asn Tyr Lys Leu Arg Ala Lys Glu Ile Arg Asn  
 35 40 45  
 Thr Cys Thr Tyr Cys Ser Val Gly Cys Gly Leu Leu Met Tyr Ser Leu  
 50 55 60  
 Gly Asp Gly Ala Lys Asn Ala Arg Glu Ala Ile Tyr His Ile Glu Gly  
 65 70 75 80  
 Asp Pro Asp His Pro Val Ser Arg Gly Ala Leu Cys Pro Lys Gly Ala  
 85 90 95  
 Gly Leu Leu Asp Tyr Val Asn Ser Glu Asn Arg Leu Arg Tyr Pro Glu  
 100 105 110  
 Tyr Arg Ala Pro Gly Ser Asp Lys Trp Gln Arg Ile Ser Trp Glu Glu  
 115 120 125  
 Ala Phe Ser Arg Ile Ala Lys Leu Met Lys Ala Asp Arg Asp Ala Asn  
 130 135 140  
 Phe Ile Glu Lys Asn Glu Gln Gly Val Thr Val Asn Arg Trp Leu Ser  
 145 150 155 160  
 Thr Gly Met Leu Cys Ala Ser Gly Ala Ser Asn Glu Thr Gly Met Leu  
 165 170 175  
 Thr Gln Lys Phe Ala Arg Ser Leu Gly Met Leu Ala Val Asp Asn Gln  
 180 185 190  
 Ala Arg Val His Gly Pro Thr Val Ala Ser Leu Ala Pro Thr Phe Gly  
 195 200 205  
 Arg Gly Ala Met Thr Asn His Trp Val Asp Ile Lys Asn Ala Asn Val  
 210 215 220  
 Val Met Val Met Gly Gly Asn Ala Ala Glu Ala His Pro Val Gly Phe  
 225 230 235 240  
 Arg Trp Ala Met Glu Ala Lys Asn Asn Asn Asp Ala Thr Leu Ile Val  
 245 250 255  
 Val Asp Pro Arg Phe Thr Arg Thr Ala Ser Val Ala Asp Ile Tyr Ala  
 260 265 270  
 Pro Ile Arg Ser Gly Thr Asp Ile Thr Phe Leu Ser Gly Val Leu Arg  
 275 280 285  
 Tyr Leu Ile Glu Asn Asn Lys Ile Asn Ala Glu Tyr Val Lys His Tyr  
 290 295 300  
 Thr Asn Ala Ser Leu Leu Val Arg Asp Asp Phe Ala Phe Glu Asp Gly  
 305 310 315 320  
 Leu Phe Ser Gly Tyr Asp Ala Glu Lys Arg Gln Tyr Asp Lys Ser Ser  
 325 330 335  
 Trp Asn Tyr Gln Leu Asp Glu Asn Gly Tyr Ala Lys Arg Asp Glu Thr  
 340 345 350  
 Leu Thr His Pro Arg Cys Val Trp Asn Leu Leu Lys Glu His Val Ser  
 355 360 365



Arg	Tyr	Thr	Pro	Asp	Val	Val	Glu	Asn	Ile	Cys	Gly	Thr	Pro	Lys	Ala
370						375					380				
Asp	Phe	Leu	Lys	Val	Cys	Glu	Val	Leu	Ala	Ser	Thr	Ser	Ala	Pro	Asp
385					390					395					400
Arg	Thr	Thr	Thr	Phe	Leu	Tyr	Ala	Leu	Gly	Trp	Thr	Gln	His	Thr	Val
				405					410					415	
Gly	Ala	Gln	Asn	Ile	Arg	Thr	Met	Ala	Met	Ile	Gln	Leu	Leu	Leu	Gly
			420					425					430		
Asn	Met	Gly	Met	Ala	Gly	Gly	Gly	Val	Asn	Ala	Leu	Arg	Gly	His	Ser
		435					440					445			
Asn	Ile	Gln	Gly	Leu	Thr	Asp	Leu	Gly	Leu	Leu	Ser	Thr	Ser	Leu	Pro
		450				455					460				
Gly	Tyr	Leu	Thr	Leu	Pro	Ser	Glu	Lys	Gln	Val	Asp	Leu	Gln	Ser	Tyr
465					470					475					480
Leu	Glu	Ala	Asn	Thr	Pro	Lys	Ala	Thr	Leu	Ala	Asp	Gln	Val	Asn	Tyr
				485						490				495	
Trp	Ser	Asn	Tyr	Pro	Lys	Phe	Phe	Val	Ser	Leu	Met	Lys	Ser	Phe	Tyr
			500					505					510		
Gly	Asp	Ala	Ala	Gln	Lys	Glu	Asn	Asn	Trp	Gly	Tyr	Asp	Trp	Leu	Pro
		515					520					525			
Lys	Trp	Asp	Gln	Thr	Tyr	Asp	Val	Ile	Lys	Tyr	Phe	Asn	Met	Met	Asp
	530					535					540				
Glu	Gly	Lys	Val	Thr	Gly	Tyr	Phe	Cys	Gln	Gly	Phe	Asn	Pro	Val	Ala
545					550					555					560
Ser	Phe	Pro	Asp	Lys	Asn	Lys	Val	Val	Ser	Cys	Leu	Ser	Lys	Leu	Lys
				565					570					575	
Tyr	Met	Val	Val	Ile	Asp	Pro	Leu	Val	Thr	Glu	Thr	Ser	Thr	Phe	Trp
			580					585					590		
Gln	Asn	His	Gly	Glu	Ser	Asn	Asp	Val	Asp	Pro	Ala	Ser	Ile	Gln	Thr
		595					600					605			
Glu	Val	Phe	Arg	Leu	Pro	Ser	Thr	Cys	Phe	Ala	Glu	Glu	Asp	Gly	Ser
	610					615					620				
Ile	Ala	Asn	Ser	Gly	Arg	Trp	Leu	Gln	Trp	His	Trp	Lys	Gly	Gln	Asp
625					630					635					640
Ala	Pro	Gly	Glu	Ala	Arg	Asn	Asp	Gly	Glu	Ile	Leu	Ala	Gly	Ile	Tyr
				645					650					655	
His	His	Leu	Arg	Glu	Leu	Tyr	Gln	Ser	Glu	Gly	Gly	Lys	Gly	Val	Glu
			660					665					670		
Pro	Leu	Met	Lys	Met	Ser	Trp	Asn	Tyr	Lys	Gln	Pro	His	Glu	Pro	Gln
		675					680					685			
Ser	Asp	Glu	Val	Ala	Lys	Glu	Asn	Asn	Gly	Tyr	Ala	Leu	Glu	Asp	Leu
		690				695					700				
Tyr	Asp	Ala	Asn	Gly	Val	Leu	Ile	Ala	Lys	Lys	Gly	Gln	Leu	Leu	Ser
705					710					715					720
Ser	Phe	Ala	His	Leu	Arg	Asp	Asp	Gly	Thr	Thr	Ala	Ser	Ser	Cys	Trp
				725					730					735	
Ile	Tyr	Thr	Gly	Ser	Trp	Thr	Glu	Gln	Gly	Asn	Gln	Met	Ala	Asn	Arg
			740					745					750		
Asp	Asn	Ser	Asp	Pro	Ser	Gly	Leu	Gly	Asn	Thr	Leu	Gly	Trp	Ala	Trp
		755					760					765			
Ala	Trp	Pro	Leu	Asn	Arg	Arg	Val	Leu	Tyr	Asn	Arg	Ala	Ser	Ala	Asp
		770				775					780				
Ile	Asn	Gly	Lys	Pro	Trp	Asp	Pro	Lys	Arg	Met	Leu	Ile	Gln	Trp	Asn
785					790					795					800
Gly	Ser	Lys	Trp	Thr	Gly	Asn	Asp	Ile	Pro	Asp	Phe	Gly	Asn	Ala	Ala
				805					810					815	
Pro	Gly	Thr	Pro	Thr	Gly	Pro	Phe	Ile	Met	Gln	Pro	Glu	Gly	Met	Gly
			820				825					830			
Arg	Leu	Phe	Ala	Ile	Asn	Lys	Met	Ala	Glu	Gly	Pro	Phe	Pro	Glu	His
		835					840					845			
Tyr	Glu	Pro	Ile	Glu	Thr	Pro	Leu	Gly	Thr	Asn	Pro	Leu	His	Pro	Asn

850	855	860
Val Val Ser Asn Pro	Val Val Arg Leu Tyr	Glu Gln Asp Ala Leu Arg
865	870	875
Met Gly Lys Lys Glu	Gln Phe Pro Tyr	Val Gly Thr Thr Tyr Arg Leu
885	890	895
Thr Glu His Phe His Thr	Trp Thr Lys His Ala	Leu Leu Asn Ala Ile
900	905	910
Ala Gln Pro Glu Gln Phe	Val Glu Ile Ser Glu	Thr Leu Ala Ala Ala
915	920	925
Lys Gly Ile Asn Asn Gly	Asp Arg Val Thr Val	Ser Ser Lys Arg Gly
930	935	940
Phe Ile Arg Ala Val Ala	Val Val Thr Arg Arg	Leu Lys Pro Leu Asn
945	950	955
Val Asn Gly Gln Gln Val	Glu Thr Val Gly Ile	Pro Ile His Trp Gly
965	970	975
Phe Glu Gly Val Ala Arg	Lys Gly Tyr Ile Ala	Asn Thr Leu Thr Pro
980	985	990
Asn Val Gly Asp Ala Asn	Ser Gln Thr Pro Glu	Tyr Lys Ala Phe Leu
995	1000	1005
Val Asn Ile Glu Lys Ala		
1010		

<210> 267  
 <211> 294  
 <212> PRT  
 <213> E. Coli

<400> 267

Met Ala Met Glu Thr Gln Asp Ile Ile	Lys Arg Ser Ala Thr Asn Ser
1	5 10 15
Ile Thr Pro Pro Ser Gln Val Arg Asp Tyr	Lys Ala Glu Val Ala Lys
20	25 30
Leu Ile Asp Val Ser Thr Cys Ile Gly Cys	Lys Ala Cys Gln Val Ala
35	40 45
Cys Ser Glu Trp Asn Asp Ile Arg Asp Glu	Val Gly His Cys Val Gly
50	55 60
Val Tyr Asp Asn Pro Ala Asp Leu Ser Ala	Lys Ser Trp Thr Val Met
65	70 75 80
Arg Phe Ser Glu Thr Glu Gln Asn Gly Lys	Leu Glu Trp Leu Ile Arg
85	90 95
Lys Asp Gly Cys Met His Cys Glu Asp Pro	Gly Cys Leu Lys Ala Cys
100	105 110
Pro Ser Ala Gly Ala Ile Ile Gln Tyr Ala	Asn Gly Ile Val Asp Phe
115	120 125
Gln Ser Glu Asn Cys Ile Gly Cys Gly Tyr	Cys Ile Ala Gly Cys Pro
130	135 140
Phe Asn Ile Pro Arg Leu Asn Lys Glu Asp	Asn Arg Val Tyr Lys Cys
145	150 155 160
Thr Leu Cys Val Asp Arg Val Ser Val Gly	Gln Glu Pro Ala Cys Val
165	170 175
Lys Thr Cys Pro Thr Gly Ala Ile His Phe	Gly Thr Lys Lys Glu Met
180	185 190
Leu Glu Leu Ala Glu Gln Arg Val Ala Lys	Leu Lys Ala Arg Gly Tyr
195	200 205
Glu His Ala Gly Val Tyr Asn Pro Glu Gly	Val Gly Thr His Val
210	215 220
Met Tyr Val Leu His His Ala Asp Gln Pro	Glu Leu Tyr His Gly Leu
225	230 235 240
Pro Lys Asp Pro Lys Ile Asp Thr Ser Val	Ser Leu Trp Lys Gly Ala
245	250 255
Leu Lys Pro Leu Ala Ala Ala Gly Phe Ile	Ala Thr Phe Ala Gly Leu

260 265 270  
 Ile Phe His Tyr Ile Gly Ile Gly Pro Asn Lys Glu Val Asp Asp Asp  
 275 280 285  
 Glu Glu Asp His His Glu  
 290

<210> 268  
 <211> 217  
 <212> PRT  
 <213> E. Coli

<400> 268  
 Met Ser Lys Ser Lys Met Ile Val Arg Thr Lys Phe Ile Asp Arg Ala  
 1 5 10 15  
 Cys His Trp Thr Val Val Ile Cys Phe Phe Leu Val Ala Leu Ser Gly  
 20 25 30  
 Ile Ser Phe Phe Phe Pro Thr Leu Gln Trp Leu Thr Gln Thr Phe Gly  
 35 40 45  
 Thr Pro Gln Met Gly Arg Ile Leu His Pro Phe Phe Gly Ile Ala Ile  
 50 55 60  
 Phe Val Ala Leu Met Phe Met Phe Val Arg Phe Val His His Asn Ile  
 65 70 75 80  
 Pro Asp Lys Lys Asp Ile Pro Trp Leu Leu Asn Ile Val Glu Val Leu  
 85 90 95  
 Lys Gly Asn Glu His Lys Val Ala Asp Val Gly Lys Tyr Asn Ala Gly  
 100 105 110  
 Gln Lys Met Met Phe Trp Ser Ile Met Ser Met Ile Phe Val Leu Leu  
 115 120 125  
 Val Thr Gly Val Ile Ile Trp Arg Pro Tyr Phe Ala Gln Tyr Phe Pro  
 130 135 140  
 Met Gln Val Val Arg Tyr Ser Leu Leu Ile His Ala Ala Ala Gly Ile  
 145 150 155 160  
 Ile Leu Ile His Ala Ile Leu Ile His Met Tyr Met Ala Phe Trp Val  
 165 170 175  
 Lys Gly Ser Ile Lys Gly Met Ile Glu Gly Lys Val Ser Arg Arg Trp  
 180 185 190  
 Ala Lys Lys His His Pro Arg Trp Tyr Arg Glu Ile Glu Lys Ala Glu  
 195 200 205  
 Ala Lys Lys Glu Ser Glu Glu Gly Ile  
 210 215

<210> 269  
 <211> 86  
 <212> PRT  
 <213> E. Coli

<400> 269  
 Met Ala Leu Leu Ile Thr Lys Lys Cys Ile Asn Cys Asp Met Cys Glu  
 1 5 10 15  
 Pro Glu Cys Pro Asn Glu Ala Ile Ser Met Gly Asp His Ile Tyr Glu  
 20 25 30  
 Ile Asn Ser Asp Lys Cys Thr Glu Cys Val Gly His Tyr Glu Thr Pro  
 35 40 45  
 Thr Cys Gln Lys Val Cys Pro Ile Pro Asn Thr Ile Val Lys Asp Pro  
 50 55 60  
 Ala His Val Glu Thr Glu Glu Gln Leu Trp Asp Lys Phe Val Leu Met  
 65 70 75 80  
 His His Ala Asp Lys Ile  
 85

<210> 270  
 <211> 400  
 <212> PRT  
 <213> E. Coli

<400> 270  
 Met Gln Ser Val Asp Val Ala Ile Val Gly Gly Gly Met Val Gly Leu  
 1 5 10 15  
 Ala Val Ala Cys Gly Leu Gln Gly Ser Gly Leu Arg Val Ala Val Leu  
 20 25 30  
 Glu Gln Arg Val Gln Glu Pro Leu Ala Ala Asn Ala Pro Gln Leu  
 35 40 45  
 Arg Val Ser Ala Ile Asn Ala Ala Ser Glu Lys Leu Leu Thr Arg Leu  
 50 55 60  
 Gly Val Trp Gln Asp Ile Leu Ser Arg Arg Ala Ser Cys Tyr His Gly  
 65 70 75 80  
 Met Glu Val Trp Asp Lys Asp Ser Phe Gly His Ile Ser Phe Asp Asp  
 85 90 95  
 Gln Ser Met Gly Tyr Ser His Leu Gly His Ile Val Glu Asn Ser Val  
 100 105 110  
 Ile His Tyr Ala Leu Trp Asn Lys Ala His Gln Ser Ser Asp Ile Thr  
 115 120 125  
 Leu Leu Ala Pro Ala Glu Leu Gln Gln Val Ala Trp Gly Glu Asn Glu  
 130 135 140  
 Thr Phe Leu Thr Leu Lys Asp Gly Ser Met Leu Thr Ala Arg Leu Val  
 145 150 155 160  
 Ile Gly Ala Asp Gly Ala Asn Ser Trp Leu Arg Asn Lys Ala Asp Ile  
 165 170 175  
 Pro Leu Thr Phe Trp Asp Tyr Gln His His Ala Leu Val Ala Thr Ile  
 180 185 190  
 Arg Thr Glu Glu Pro His Asp Ala Val Ala Arg Gln Val Phe His Gly  
 195 200 205  
 Glu Gly Ile Leu Ala Phe Leu Pro Leu Ser Asp Pro His Leu Cys Ser  
 210 215 220  
 Ile Val Trp Ser Leu Ser Pro Glu Glu Ala Gln Arg Met Gln Gln Ala  
 225 230 235 240  
 Ser Glu Asp Glu Phe Asn Arg Ala Leu Asn Ile Ala Phe Asp Asn Arg  
 245 250 255  
 Leu Gly Leu Cys Lys Val Glu Ser Ala Arg Gln Val Phe Pro Leu Thr  
 260 265 270  
 Gly Arg Tyr Ala Arg Gln Phe Ala Ser His Arg Leu Ala Leu Val Gly  
 275 280 285  
 Asp Ala Ala His Thr Ile His Pro Leu Ala Gly Gln Gly Val Asn Leu  
 290 295 300  
 Gly Phe Met Asp Ala Ala Glu Leu Ile Ala Glu Leu Lys Arg Leu His  
 305 310 315 320  
 Arg Gln Gly Lys Asp Ile Gly Gln Tyr Ile Tyr Leu Arg Arg Tyr Glu  
 325 330 335  
 Arg Ser Arg Lys His Ser Ala Ala Leu Met Leu Ala Gly Met Gln Gly  
 340 345 350  
 Phe Arg Asp Leu Phe Ser Gly Thr Asn Pro Ala Lys Lys Leu Leu Arg  
 355 360 365  
 Asp Ile Gly Leu Lys Leu Ala Asp Thr Leu Pro Gly Val Lys Pro Gln  
 370 375 380  
 Leu Ile Arg Gln Ala Met Gly Leu Asn Asp Leu Pro Glu Trp Leu Arg  
 385 390 395 400

<210> 271

<211> 392  
 <212> PRT  
 <213> E. Coli

<400> 271  
 Met Ser Val Ile Ile Val Gly Gly Gly Met Ala Gly Ala Thr Leu Ala  
 1 5 10 15  
 Leu Ala Ile Ser Arg Leu Ser His Gly Ala Leu Pro Val His Leu Ile  
 20 25 30  
 Glu Ala Thr Ala Pro Glu Ser His Ala His Pro Gly Phe Asp Gly Arg  
 35 40 45  
 Ala Ile Ala Leu Ala Ala Gly Thr Cys Gln Gln Leu Ala Arg Ile Gly  
 50 55 60  
 Val Trp Gln Ser Leu Ala Asp Cys Ala Thr Ala Ile Thr Thr Val His  
 65 70 75 80  
 Val Ser Asp Arg Gly His Ala Gly Phe Val Thr Leu Ala Ala Glu Asp  
 85 90 95  
 Tyr Gln Leu Ala Ala Leu Gly Gln Val Val Glu Leu His Asn Val Gly  
 100 105 110  
 Gln Arg Leu Phe Ala Leu Leu Arg Lys Ala Pro Gly Val Thr Leu His  
 115 120 125  
 Cys Pro Asp Arg Val Ala Asn Val Ala Arg Thr Gln Ser His Val Glu  
 130 135 140  
 Val Thr Leu Glu Ser Gly Glu Thr Leu Thr Gly Arg Val Leu Val Ala  
 145 150 155 160  
 Ala Asp Gly Thr His Ser Ala Leu Ala Thr Ala Cys Gly Val Asp Trp  
 165 170 175  
 Gln Gln Glu Pro Tyr Glu Gln Leu Ala Val Ile Ala Asn Val Ala Thr  
 180 185 190  
 Ser Val Ala His Glu Gly Arg Ala Phe Glu Arg Phe Thr Gln His Gly  
 195 200 205  
 Pro Leu Ala Met Leu Pro Met Ser Asp Gly Arg Cys Ser Leu Val Trp  
 210 215 220  
 Cys His Pro Leu Glu Arg Arg Glu Glu Val Leu Ser Trp Ser Asp Glu  
 225 230 235 240  
 Lys Phe Cys Arg Glu Leu Gln Ser Ala Phe Gly Trp Arg Leu Gly Lys  
 245 250 255  
 Ile Thr His Ala Gly Lys Arg Ser Ala Tyr Pro Leu Ala Leu Thr His  
 260 265 270  
 Ala Ala Arg Ser Ile Thr His Arg Thr Val Leu Val Gly Asn Ala Ala  
 275 280 285  
 Gln Thr Leu His Pro Ile Ala Gly Gln Gly Phe Asn Leu Gly Met Arg  
 290 295 300  
 Asp Val Met Ser Leu Ala Glu Thr Leu Thr Gln Ala Gln Glu Arg Gly  
 305 310 315 320  
 Glu Asp Met Gly Asp Tyr Gly Val Leu Cys Arg Tyr Gln Gln Arg Arg  
 325 330 335  
 Gln Ser Asp Arg Glu Ala Thr Ile Gly Val Thr Asp Ser Leu Val His  
 340 345 350  
 Leu Phe Ala Asn Arg Trp Ala Pro Leu Val Val Gly Arg Asn Ile Gly  
 355 360 365  
 Leu Met Thr Met Glu Leu Phe Thr Pro Ala Arg Asp Val Leu Ala Gln  
 370 375 380  
 Arg Thr Leu Gly Trp Val Ala Arg  
 385 390

<210> 272  
 <211> 441  
 <212> PRT  
 <213> E. Coli

&lt;400&gt; 272

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Met Ser Glu Ile Ser Arg Gln Glu Phe Gln Arg Arg Arg Gln Ala Leu
 1      5      10      15
Val Glu Gln Met Gln Pro Gly Ser Ala Ala Leu Ile Phe Ala Ala Pro
 20      25      30
Glu Val Thr Arg Ser Ala Asp Ser Glu Tyr Pro Tyr Arg Gln Asn Ser
 35      40      45
Asp Phe Trp Tyr Phe Thr Gly Phe Asn Glu Pro Glu Ala Val Leu Val
 50      55      60
Leu Ile Lys Ser Asp Asp Thr His Asn His Ser Val Leu Phe Asn Arg
 65      70      75      80
Val Arg Asp Leu Thr Ala Glu Ile Trp Phe Gly Arg Arg Leu Gly Gln
 85      90      95
Asp Ala Ala Pro Glu Lys Leu Gly Val Asp Arg Ala Leu Ala Phe Ser
 100     105     110
Glu Ile Asn Gln Gln Leu Tyr Gln Leu Leu Asn Gly Leu Asp Val Val
 115     120     125
Tyr His Ala Gln Gly Glu Tyr Ala Tyr Ala Asp Val Ile Val Asn Ser
 130     135     140
Ala Leu Glu Lys Leu Arg Lys Gly Ser Arg Gln Asn Leu Thr Ala Pro
 145     150     155     160
Ala Thr Met Ile Asp Trp Arg Pro Val Val His Glu Met Arg Leu Phe
 165     170     175
Lys Ser Pro Glu Glu Ile Ala Val Leu Arg Arg Ala Gly Glu Ile Thr
 180     185     190
Ala Met Ala His Thr Arg Ala Met Glu Lys Cys Arg Pro Gly Met Phe
 195     200     205
Glu Tyr His Leu Glu Gly Glu Ile His His Glu Phe Asn Arg His Gly
 210     215     220
Ala Arg Tyr Pro Ser Tyr Asn Thr Ile Val Gly Ser Gly Glu Asn Gly
 225     230     235     240
Cys Ile Leu His Tyr Thr Glu Asn Glu Cys Glu Met Arg Asp Gly Asp
 245     250     255
Leu Val Leu Ile Asp Ala Gly Cys Glu Tyr Lys Gly Tyr Ala Gly Asp
 260     265     270
Ile Thr Arg Thr Phe Pro Val Asn Gly Lys Phe Thr Gln Ala Gln Arg
 275     280     285
Glu Ile Tyr Asp Ile Val Leu Glu Ser Leu Glu Thr Ser Leu Arg Leu
 290     295     300
Tyr Arg Pro Gly Thr Ser Ile Leu Glu Val Thr Gly Glu Val Val Arg
 305     310     315     320
Ile Met Val Ser Gly Leu Val Lys Leu Gly Ile Leu Lys Gly Asp Val
 325     330     335
Asp Glu Leu Ile Ala Gln Asn Ala His Arg Pro Phe Phe Met His Gly
 340     345     350
Leu Ser His Trp Leu Gly Leu Asp Val His Asp Val Gly Val Tyr Gly
 355     360     365
Gln Asp Arg Ser Arg Ile Leu Glu Pro Gly Met Val Leu Thr Val Glu
 370     375     380
Pro Gly Leu Tyr Ile Ala Pro Asp Ala Glu Val Pro Glu Gln Tyr Arg
 385     390     395     400
Gly Ile Gly Ile Arg Ile Glu Asp Asp Ile Val Ile Thr Glu Thr Gly
 405     410     415
Asn Glu Asn Leu Thr Ala Ser Val Val Lys Lys Pro Glu Glu Ile Glu
 420     425     430
Ala Leu Met Val Ala Ala Arg Lys Gln
 435     440

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&lt;210&gt; 273

<211> 194  
 <212> PRT  
 <213> E. Coli

<400> 273  
 Met Leu Met Ser Ile Gln Asn Glu Met Pro Gly Tyr Asn Glu Met Asn  
 1 5 10 15  
 Gln Tyr Leu Asn Gln Gln Gly Thr Gly Leu Thr Pro Ala Glu Met His  
 20 25 30  
 Gly Leu Ile Ser Gly Met Ile Cys Gly Gly Asn Asp Asp Ser Ser Trp  
 35 40 45  
 Leu Pro Leu Leu His Asp Leu Thr Asn Glu Gly Met Ala Phe Gly His  
 50 55 60  
 Glu Leu Ala Gln Ala Leu Arg Lys Met His Ser Ala Thr Ser Asp Ala  
 65 70 75 80  
 Leu Gln Asp Asp Gly Phe Leu Phe Gln Leu Tyr Leu Pro Asp Gly Asp  
 85 90 95  
 Asp Val Ser Val Phe Asp Arg Ala Asp Ala Leu Ala Gly Trp Val Asn  
 100 105 110  
 His Phe Leu Leu Gly Leu Gly Val Thr Gln Pro Lys Leu Asp Lys Val  
 115 120 125  
 Thr Gly Glu Thr Gly Glu Ala Ile Asp Asp Leu Arg Asn Ile Ala Gln  
 130 135 140  
 Leu Gly Tyr Asp Glu Asp Glu Asp Gln Glu Glu Leu Glu Met Ser Leu  
 145 150 155 160  
 Glu Glu Ile Ile Glu Tyr Val Arg Val Ala Ala Leu Leu Cys His Asp  
 165 170 175  
 Thr Phe Thr His Pro Gln Pro Thr Ala Pro Glu Val Gln Lys Pro Thr  
 180 185 190  
 Leu His

<210> 274  
 <211> 120  
 <212> PRT  
 <213> E. Coli

<400> 274  
 Met Leu Lys Leu Phe Ala Lys Tyr Thr Ser Ile Gly Val Leu Asn Thr  
 1 5 10 15  
 Leu Ile His Trp Val Val Phe Gly Val Cys Ile Tyr Val Ala His Thr  
 20 25 30  
 Asn Gln Ala Leu Ala Asn Phe Ala Gly Phe Val Val Ala Val Ser Phe  
 35 40 45  
 Ser Phe Phe Ala Asn Ala Lys Phe Thr Phe Lys Ala Ser Thr Thr Thr  
 50 55 60  
 Met Arg Tyr Met Leu Tyr Val Gly Phe Met Gly Thr Leu Ser Ala Thr  
 65 70 75 80  
 Val Gly Trp Ala Ala Asp Arg Cys Ala Leu Pro Pro Met Ile Thr Leu  
 85 90 95  
 Val Thr Phe Ser Ala Ile Ser Leu Val Cys Gly Phe Val Tyr Ser Lys  
 100 105 110  
 Phe Ile Val Phe Arg Asp Ala Lys  
 115 120

<210> 275  
 <211> 306  
 <212> PRT  
 <213> E. Coli

&lt;400&gt; 275

Met Lys Ile Ser Leu Val Val Pro Val Phe Asn Glu Glu Glu Ala Ile  
 1 5 10 15  
 Pro Ile Phe Tyr Lys Thr Val Arg Glu Phe Glu Glu Leu Lys Ser Tyr  
 20 25 30  
 Glu Val Glu Ile Val Phe Ile Asn Asp Gly Ser Lys Asp Ala Thr Glu  
 35 40 45  
 Ser Ile Ile Asn Ala Leu Ala Val Ser Asp Pro Leu Val Val Pro Leu  
 50 55 60  
 Ser Phe Thr Arg Asn Phe Gly Lys Glu Pro Ala Leu Phe Ala Gly Leu  
 65 70 75 80  
 Asp His Ala Thr Gly Asp Ala Ile Ile Pro Ile Asp Val Asp Leu Gln  
 85 90 95  
 Asp Pro Ile Glu Val Ile Pro His Leu Ile Glu Lys Trp Gln Ala Gly  
 100 105 110  
 Ala Asp Met Val Leu Ala Lys Arg Ser Asp Arg Ser Thr Asp Gly Arg  
 115 120 125  
 Leu Lys Arg Lys Thr Ala Glu Trp Phe Tyr Lys Leu His Asn Lys Ile  
 130 135 140  
 Ser Asn Pro Lys Ile Glu Glu Asn Val Gly Asp Phe Arg Leu Met Ser  
 145 150 155 160  
 Arg Asp Val Val Glu Asn Ile Lys Leu Met Pro Glu Arg Asn Leu Phe  
 165 170 175  
 Met Lys Gly Ile Leu Ser Trp Val Gly Gly Lys Thr Asp Ile Val Glu  
 180 185 190  
 Tyr Val Arg Ala Glu Arg Ile Ala Gly Asp Thr Lys Phe Asn Gly Trp  
 195 200 205  
 Lys Leu Trp Asn Leu Ala Leu Glu Gly Ile Thr Ser Phe Ser Thr Phe  
 210 215 220  
 Pro Leu Arg Ile Trp Thr Tyr Ile Gly Leu Val Val Ala Ser Val Ala  
 225 230 235 240  
 Phe Ile Tyr Gly Ala Trp Met Ile Leu Asp Thr Ile Ile Phe Gly Asn  
 245 250 255  
 Ala Val Arg Gly Tyr Pro Ser Leu Leu Val Ser Ile Leu Phe Leu Gly  
 260 265 270  
 Gly Ile Gln Met Ile Gly Ile Gly Val Leu Gly Glu Tyr Ile Gly Arg  
 275 280 285  
 Thr Tyr Ile Glu Thr Lys Lys Arg Pro Lys Tyr Ile Ile Lys Arg Val  
 290 295 300  
 Lys Lys  
 305

&lt;210&gt; 276

&lt;211&gt; 443

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 276

Met Asn Lys Ala Ile Lys Val Ser Leu Tyr Ile Ser Phe Val Leu Ile  
 1 5 10 15  
 Ile Cys Ala Leu Ser Lys Asn Ile Met Met Leu Asn Thr Ser Asp Phe  
 20 25 30  
 Gly Arg Ala Ile Lys Pro Leu Ile Glu Asp Ile Pro Ala Phe Thr Tyr  
 35 40 45  
 Asp Leu Pro Leu Leu Tyr Lys Leu Lys Gly His Ile Asp Ser Ile Asp  
 50 55 60  
 Ser Tyr Glu Tyr Ile Ser Ser Tyr Ser Tyr Ile Leu Tyr Thr Tyr Val  
 65 70 75 80  
 Leu Phe Ile Ser Ile Phe Thr Glu Tyr Leu Asp Ala Arg Val Leu Ser  
 85 90 95



Leu Phe Leu Lys Val Ile Tyr Ile Tyr Ser Leu Tyr Ala Ile Phe Thr  
 100 105 110  
 Ser Tyr Ile Lys Thr Glu Arg Tyr Val Thr Leu Phe Thr Phe Phe Ile  
 115 120 125  
 Leu Ala Phe Leu Met Cys Ser Ser Ser Thr Leu Ser Met Phe Ala Ser  
 130 135 140  
 Phe Tyr Gln Glu Gln Ile Val Ile Ile Phe Leu Pro Phe Leu Val Tyr  
 145 150 155 160  
 Ser Leu Thr Cys Lys Asn Asn Lys Ser Met Leu Leu Leu Phe Phe Ser  
 165 170 175  
 Leu Leu Ile Ile Ser Thr Ala Lys Asn Gln Phe Ile Leu Thr Pro Leu  
 180 185 190  
 Ile Val Tyr Ser Tyr Tyr Ile Phe Phe Asp Arg His Lys Leu Ile Ile  
 195 200 205  
 Lys Ser Val Ile Cys Val Val Cys Leu Leu Ala Ser Ile Phe Ala Ile  
 210 215 220  
 Ser Tyr Ser Lys Gly Val Val Glu Leu Asn Lys Tyr His Ala Thr Tyr  
 225 230 235 240  
 Phe Gly Ser Tyr Leu Tyr Met Lys Asn Asn Gly Tyr Lys Met Pro Ser  
 245 250 255  
 Tyr Val Asp Asp Lys Cys Val Gly Leu Asp Ala Trp Gly Asn Lys Phe  
 260 265 270  
 Asp Ile Ser Phe Gly Ala Thr Pro Thr Glu Val Gly Thr Glu Cys Phe  
 275 280 285  
 Glu Ser His Lys Asp Glu Thr Phe Ser Asn Ala Leu Phe Leu Leu Val  
 290 295 300  
 Ser Lys Pro Ser Thr Ile Phe Lys Leu Pro Phe Asp Asp Gly Val Met  
 305 310 315 320  
 Ser Gln Tyr Lys Glu Asn Tyr Phe His Val Tyr Lys Lys Leu His Val  
 325 330 335  
 Ile Tyr Gly Glu Ser Asn Ile Leu Thr Thr Ile Thr Asn Ile Lys Asp  
 340 345 350  
 Asn Ile Phe Lys Asn Ile Arg Phe Ile Ser Leu Leu Leu Phe Phe Ile  
 355 360 365  
 Ala Ser Ile Phe Ile Arg Asn Asn Lys Ile Lys Ala Ser Leu Phe Val  
 370 375 380  
 Val Ser Leu Phe Gly Ile Ser Gln Phe Tyr Val Ser Phe Phe Gly Glu  
 385 390 395 400  
 Gly Tyr Arg Asp Leu Ser Lys His Leu Phe Gly Met Tyr Phe Ser Phe  
 405 410 415  
 Asp Leu Cys Leu Tyr Ile Thr Val Val Phe Leu Ile Tyr Lys Ile Ile  
 420 425 430  
 Gln Arg Asn Gln Asp Asn Ser Asp Val Lys His  
 435 440

&lt;210&gt; 277

&lt;211&gt; 82

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 277

Met Gly Ile Leu Ser Trp Ile Ile Phe Gly Leu Ile Ala Gly Ile Leu  
 1 5 10 15  
 Ala Lys Trp Ile Met Pro Gly Lys Asp Gly Gly Gly Phe Phe Met Thr  
 20 25 30  
 Ile Leu Leu Gly Ile Val Gly Ala Val Val Gly Gly Trp Ile Ser Thr  
 35 40 45  
 Leu Phe Gly Phe Gly Lys Val Asp Gly Phe Asn Phe Gly Ser Phe Val  
 50 55 60

Val Ala Val Ile Gly Ala Ile Val Val Leu Phe Ile Tyr Arg Lys Ile  
 65 70 75 80  
 Lys Ser

<210> 278  
 <211> 60  
 <212> PRT  
 <213> E. Coli

<400> 278  
 Met Gly Lys Ala Thr Tyr Thr Val Thr Val Thr Asn Asn Ser Asn Gly  
 1 5 10 15  
 Val Ser Val Asp Tyr Glu Thr Glu Thr Pro Met Thr Leu Leu Val Pro  
 20 25 30  
 Glu Val Ala Ala Glu Val Ile Lys Asp Leu Val Asn Thr Val Arg Ser  
 35 40 45  
 Tyr Asp Thr Glu Asn Glu His Asp Val Cys Gly Trp  
 50 55 60

<210> 279  
 <211> 119  
 <212> PRT  
 <213> E. Coli

<400> 279  
 Met Leu Gln Ile Pro Gln Asn Tyr Ile His Thr Arg Ser Thr Pro Phe  
 1 5 10 15  
 Trp Asn Lys Gln Thr Ala Pro Ala Gly Ile Phe Glu Arg His Leu Asp  
 20 25 30  
 Lys Gly Thr Arg Pro Gly Val Tyr Pro Arg Leu Ser Val Met His Gly  
 35 40 45  
 Ala Val Lys Tyr Leu Gly Tyr Ala Asp Glu His Ser Ala Glu Pro Asp  
 50 55 60  
 Gln Val Ile Leu Ile Glu Ala Gly Gln Phe Ala Val Phe Pro Pro Glu  
 65 70 75 80  
 Lys Trp His Asn Ile Glu Ala Met Thr Asp Thr Tyr Phe Asn Ile  
 85 90 95  
 Asp Phe Phe Val Ala Pro Glu Val Leu Met Glu Gly Ala Gln Gln Arg  
 100 105 110  
 Lys Val Ile His Asn Gly Lys  
 115

<210> 280  
 <211> 246  
 <212> PRT  
 <213> E. Coli

<400> 280  
 Met Lys Phe Lys Val Ile Ala Leu Ala Ala Leu Met Gly Ile Ser Gly  
 1 5 10 15  
 Met Ala Ala Gln Ala Asn Glu Leu Pro Asp Gly Pro His Ile Val Thr  
 20 25 30  
 Ser Gly Thr Ala Ser Val Asp Ala Val Pro Asp Ile Ala Thr Leu Ala  
 35 40 45  
 Ile Glu Val Asn Val Ala Ala Lys Asp Ala Ala Thr Ala Lys Lys Gln  
 50 55 60  
 Ala Asp Glu Arg Val Ala Gln Tyr Ile Ser Phe Leu Glu Leu Asn Gln

65	Ile	Ala	Lys	Lys	Asp	85	Ile	Ser	Ser	Ala	Asn	Leu	Arg	Thr	Gln	Pro	Asp	80
	Tyr	Asp	Tyr	Gln	Asp	100	Gly	Lys	Ser	Ile	Leu	Lys	Gly	Tyr	Arg	Ala	Val	
	Arg	Thr	Val	Glu	Val	115	Thr	Leu	Arg	Gln	Leu	Asp	Lys	Leu	Asn	Ser	Leu	
	Leu	Asp	Gly	Ala	Leu	130	Lys	Ala	Gly	Leu	Asn	Glu	Ile	Arg	Ser	Val	Ser	
	Leu	Gly	Val	Ala	Gln	145	Pro	Asp	Ala	Tyr	Lys	Asp	Lys	Ala	Arg	Lys	Ala	
	Ala	Ile	Asp	Asn	Ala	165	Ile	His	Gln	Ala	Gln	Glu	Leu	Ala	Asn	Gly	Phe	
	His	Arg	Lys	Leu	Gly	180	Pro	Val	Tyr	Ser	Val	Arg	Tyr	His	Val	Ser	Asn	
	Tyr	Gln	Pro	Ser	Pro	195	Met	Val	Arg	Met	Met	Lys	Ala	Asp	Ala	Ala	Pro	
	Val	Ser	Ala	Gln	Glu	210	Thr	Tyr	Glu	Gln	Ala	Ala	Ile	Gln	Phe	Asp	Asp	
	Gln	Val	Asp	Val	Val	225	Phe	Gln	Leu	Glu	Pro	Val	Asp	Gln	Gln	Pro	Ala	
	Lys	Thr	Pro	Ala	Ala	245	Gln											

<210> 281  
 <211> 464  
 <212> PRT  
 <213> E. Coli

<400> 281

Met	Leu	Leu	Leu	Asp	Ala	Cys	Ser	Gln	Met	Cys	Pro	Ser	Phe	Arg	Arg		
1				5				10						15			
Phe	Gln	Thr	Val	Phe	His	Asn	Ser	Ser	Ile	Phe	Leu	Pro	Tyr	Trp	Leu		
			20					25					30				
Ala	Thr	Leu	Val	Ser	Phe	Arg	Glu	Thr	Phe	Gln	Glu	Glu	Lys	Leu	Leu		
			35				40					45					
Thr	Met	Lys	Gly	Ser	Tyr	Lys	Ser	Arg	Trp	Val	Ile	Val	Ile	Val	Val		
			50			55				60							
Val	Ile	Ala	Ala	Ile	Ala	Ala	Phe	Trp	Phe	Trp	Gln	Gly	Arg	Asn	Asp		
65				70					75					80			
Ser	Arg	Ser	Ala	Ala	Pro	Gly	Ala	Thr	Lys	Gln	Ala	Gln	Gln	Ser	Pro		
			85					90					95				
Ala	Gly	Gly	Arg	Arg	Gly	Met	Arg	Ser	Gly	Pro	Leu	Ala	Pro	Val	Gln		
			100					105					110				
Ala	Ala	Thr	Ala	Val	Glu	Gln	Ala	Val	Pro	Arg	Tyr	Leu	Thr	Gly	Leu		
			115				120						125				
Gly	Thr	Ile	Thr	Ala	Ala	Asn	Thr	Val	Thr	Val	Arg	Ser	Arg	Val	Asp		
			130			135					140						
Gly	Gln	Leu	Ile	Ala	Leu	His	Phe	Gln	Glu	Gly	Gln	Gln	Val	Lys	Ala		
145				150					155					160			
Gly	Asp	Leu	Leu	Ala	Glu	Ile	Asp	Pro	Ser	Gln	Phe	Lys	Val	Ala	Leu		
			165					170					175				
Ala	Gln	Ala	Gln	Gly	Gln	Leu	Ala	Lys	Asp	Lys	Ala	Thr	Leu	Ala	Asn		
			180				185						190				
Ala	Arg	Arg	Asp	Leu	Ala	Arg	Tyr	Gln	Gln	Leu	Ala	Lys	Thr	Asn	Leu		
			195				200					205					
Val	Ser	Arg	Gln	Glu	Leu	Asp	Ala	Gln	Gln	Ala	Leu	Val	Ser	Glu	Thr		
			210			215						220					
Glu	Gly	Thr	Ile	Lys	Ala	Asp	Glu	Ala	Ser	Val	Ala	Ser	Ala	Gln	Leu		
225				230					235					240			

Gln Leu Asp Trp Ser Arg Ile Thr Ala Pro Val Asp Gly Arg Val Gly  
                   245                  250                  255  
 Leu Lys Gln Val Asp Val Gly Asn Gln Ile Ser Ser Gly Asp Thr Thr  
                   260                  265                  270  
 Gly Ile Val Val Ile Thr Gln Thr His Pro Ile Asp Leu Val Phe Thr  
                   275                  280                  285  
 Leu Pro Glu Ser Asp Ile Ala Thr Val Val Gln Ala Gln Lys Ala Gly  
                   290                  295                  300  
 Lys Pro Leu Val Val Glu Ala Trp Asp Arg Thr Asn Ser Lys Lys Leu  
                   305                  310                  315                  320  
 Ser Glu Gly Thr Leu Leu Ser Leu Asp Asn Gln Ile Asp Ala Thr Thr  
                   325                  330                  335  
 Gly Thr Ile Lys Val Lys Ala Arg Phe Asn Asn Gln Asp Asp Ala Leu  
                   340                  345                  350  
 Phe Pro Asn Gln Phe Val Asn Ala Arg Met Leu Val Asp Thr Glu Gln  
                   355                  360                  365  
 Asn Ala Val Val Ile Pro Thr Ala Ala Leu Gln Met Gly Asn Glu Gly  
                   370                  375                  380  
 His Phe Val Trp Val Leu Asn Ser Glu Asn Lys Val Ser Lys His Leu  
                   385                  390                  395                  400  
 Val Thr Pro Gly Ile Gln Asp Ser Gln Lys Val Val Ile Arg Ala Gly  
                   405                  410                  415  
 Ile Ser Ala Gly Asp Arg Val Val Thr Asp Gly Ile Asp Arg Leu Thr  
                   420                  425                  430  
 Glu Gly Ala Lys Val Glu Val Val Glu Ala Gln Ser Ala Thr Thr Pro  
                   435                  440                  445  
 Glu Glu Lys Ala Thr Ser Arg Glu Tyr Ala Lys Lys Gly Ala Arg Ser  
                   450                  455                  460

<210> 282  
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 <212> PRT  
 <213> E. Coli

<400> 282  
 Met Gln Val Leu Pro Pro Ser Ser Thr Gly Gly Pro Ser Arg Leu Phe  
   1                  5                  10                  15  
 Ile Met Arg Pro Val Ala Thr Thr Leu Met Val Ala Ile Leu Leu  
                   20                  25                  30  
 Ala Gly Ile Ile Gly Tyr Arg Ala Leu Pro Val Ser Ala Leu Pro Glu  
                   35                  40                  45  
 Val Asp Tyr Pro Thr Ile Gln Val Val Thr Leu Tyr Pro Gly Ala Ser  
                   50                  55                  60  
 Pro Asp Val Met Thr Ser Ala Val Thr Ala Pro Leu Glu Arg Gln Phe  
                   65                  70                  75                  80  
 Gly Gln Met Ser Gly Leu Lys Gln Met Ser Ser Gln Ser Ser Gly Gly  
                   85                  90                  95  
 Ala Ser Val Ile Thr Leu Gln Phe Gln Leu Thr Leu Pro Leu Asp Val  
                   100                  105                  110  
 Ala Glu Gln Glu Val Gln Ala Ala Ile Asn Ala Ala Thr Asn Leu Leu  
                   115                  120                  125  
 Pro Ser Asp Leu Pro Asn Pro Pro Val Tyr Ser Lys Val Asn Pro Ala  
                   130                  135                  140  
 Asp Pro Pro Ile Met Thr Leu Ala Val Thr Ser Thr Ala Met Pro Met  
                   145                  150                  155                  160  
 Thr Gln Val Glu Asp Met Val Glu Thr Arg Val Ala Gln Lys Ile Ser  
                   165                  170                  175  
 Gln Ile Ser Gly Val Gly Leu Val Thr Leu Ser Gly Gly Gln Arg Pro  
                   180                  185                  190  
 Ala Val Arg Val Lys Leu Asn Ala Gln Ala Ile Ala Ala Leu Gly Leu

195	200	205
Thr Ser Glu Thr Val Arg Thr Ala Ile Thr Gly Ala Asn Val Asn Ser		
210	215	220
Ala Lys Gly Ser Leu Asp Gly Pro Ser Arg Ala Val Thr Leu Ser Ala		
225	230	235
Asn Asp Gln Met Gln Ser Ala Glu Glu Tyr Arg Gln Leu Ile Ile Ala		
	245	250
Tyr Gln Asn Gly Ala Pro Ile Arg Leu Gly Asp Val Ala Thr Val Glu		
	260	265
Gln Gly Ala Glu Asn Ser Trp Leu Gly Ala Trp Ala Asn Lys Glu Gln		
	275	280
Ala Ile Val Met Asn Val Gln Arg Gln Pro Gly Ala Asn Ile Ile Ser		
	290	295
Thr Ala Asp Ser Ile Arg Gln Met Leu Pro Gln Leu Thr Glu Ser Leu		
305	310	315
Pro Lys Ser Val Lys Val Thr Val Leu Ser Asp Arg Thr Thr Asn Ile		
	325	330
Arg Ala Ser Val Asp Asp Thr Gln Phe Glu Leu Met Met Ala Ile Ala		
	340	345
Leu Val Val Met Ile Ile Tyr Leu Phe Leu Arg Asn Ile Pro Ala Thr		
	355	360
Ile Ile Pro Gly Val Ala Val Pro Leu Ser Leu Ile Gly Thr Phe Ala		
	370	375
Val Met Val Phe Leu Asp Phe Ser Ile Asn Asn Leu Thr Leu Met Ala		
385	390	395
Leu Thr Ile Ala Thr Gly Phe Val Val Asp Asp Ala Ile Val Val Ile		
	405	410
Glu Asn Ile Ser Arg Tyr Ile Glu Lys Gly Glu Lys Pro Leu Ala Ala		
	420	425
Ala Leu Lys Gly Ala Gly Glu Ile Gly Phe Thr Ile Ile Ser Leu Thr		
	435	440
Phe Ser Leu Ile Ala Val Leu Ile Pro Leu Leu Phe Met Gly Asp Ile		
	450	455
Val Gly Arg Leu Phe Arg Glu Phe Ala Ile Thr Leu Ala Val Ala Ile		
465	470	475
Leu Ile Ser Ala Val Val Ser Leu Thr Leu Thr Pro Met Met Cys Ala		
	485	490
Arg Met Leu Ser Gln Glu Ser Leu Arg Lys Gln Asn Arg Phe Ser Arg		
	500	505
Ala Ser Glu Lys Met Phe Asp Arg Ile Ile Ala Ala Tyr Gly Arg Gly		
	515	520
Leu Ala Lys Val Leu Asn His Pro Trp Leu Thr Leu Ser Val Ala Leu		
	530	535
Ser Thr Leu Leu Leu Ser Val Leu Leu Trp Val Phe Ile Pro Lys Gly		
545	550	555
Phe Phe Pro Val Gln Asp Asn Gly Ile Ile Gln Gly Thr Leu Gln Ala		
	565	570
Pro Gln Ser Ser Ser Phe Ala Asn Met Ala Gln Arg Gln Arg Gln Val		
	580	585
Ala Asp Val Ile Leu Gln Asp Pro Ala Val Gln Ser Leu Thr Ser Phe		
	595	600
Val Gly Val Asp Gly Thr Asn Pro Ser Leu Asn Ser Ala Arg Leu Gln		
	610	615
Ile Asn Leu Lys Pro Leu Asp Glu Arg Asp Asp Arg Val Gln Lys Val		
625	630	635
Ile Ala Arg Leu Gln Thr Ala Val Asp Lys Val Pro Gly Val Asp Leu		
	645	650
Phe Leu Gln Pro Thr Gln Asp Leu Thr Ile Asp Thr Gln Val Ser Arg		
	660	665
Thr Gln Tyr Gln Phe Thr Leu Gln Ala Thr Ser Leu Asp Ala Leu Ser		
	675	680
		685

Thr	Trp	Val	Pro	Gln	Leu	Met	Glu	Lys	Leu	Gln	Gln	Leu	Pro	Gln	Leu	690	695	700
Ser	Asp	Val	Ser	Ser	Asp	Trp	Gln	Asp	Lys	Gly	Leu	Val	Ala	Tyr	Val	705	710	715
Asn	Val	Asp	Arg	Asp	Ser	Ala	Ser	Arg	Leu	Gly	Ile	Ser	Met	Ala	Asp	725	730	735
Val	Asp	Asn	Ala	Leu	Tyr	Asn	Ala	Phe	Gly	Gln	Arg	Leu	Ile	Ser	Thr	740	745	750
Ile	Tyr	Thr	Gln	Ala	Asn	Gln	Tyr	Arg	Val	Val	Leu	Glu	His	Asn	Thr	755	760	765
Glu	Asn	Thr	Pro	Gly	Leu	Ala	Ala	Leu	Asp	Thr	Ile	Arg	Leu	Thr	Ser	770	775	780
Ser	Asp	Gly	Gly	Val	Val	Pro	Leu	Ser	Ser	Ile	Ala	Lys	Ile	Glu	Gln	785	790	795
Arg	Phe	Ala	Pro	Leu	Ser	Ile	Asn	His	Leu	Asp	Gln	Phe	Pro	Val	Thr	805	810	815
Thr	Ile	Ser	Phe	Asn	Val	Pro	Asp	Asn	Tyr	Ser	Leu	Gly	Asp	Ala	Val	820	825	830
Gln	Ala	Ile	Met	Asp	Thr	Glu	Lys	Thr	Leu	Asn	Leu	Pro	Val	Asp	Ile	835	840	845
Thr	Thr	Gln	Phe	Gln	Gly	Ser	Thr	Leu	Ala	Phe	Gln	Ser	Ala	Leu	Gly	850	855	860
Ser	Thr	Val	Trp	Leu	Ile	Val	Ala	Ala	Val	Val	Ala	Met	Tyr	Ile	Val	865	870	875
Leu	Gly	Ile	Leu	Tyr	Glu	Ser	Phe	Ile	His	Pro	Ile	Thr	Ile	Leu	Ser	885	890	895
Thr	Leu	Pro	Thr	Ala	Gly	Val	Gly	Ala	Leu	Leu	Ala	Leu	Leu	Ile	Ala	900	905	910
Gly	Ser	Glu	Leu	Asp	Val	Ile	Ala	Ile	Ile	Gly	Ile	Ile	Leu	Leu	Ile	915	920	925
Gly	Ile	Val	Lys	Lys	Asn	Ala	Ile	Met	Met	Ile	Asp	Phe	Ala	Leu	Ala	930	935	940
Ala	Glu	Arg	Glu	Gln	Gly	Met	Ser	Pro	Arg	Glu	Ala	Ile	Tyr	Gln	Ala	945	950	955
Cys	Leu	Leu	Arg	Phe	Arg	Pro	Ile	Leu	Met	Thr	Thr	Leu	Ala	Ala	Leu	965	970	975
Leu	Gly	Ala	Leu	Pro	Leu	Met	Leu	Ser	Thr	Gly	Val	Gly	Ala	Glu	Leu	980	985	990
Arg	Arg	Pro	Leu	Gly	Ile	Gly	Met	Val	Gly	Gly	Leu	Ile	Val	Ser	Gln	995	1000	1005
Val	Leu	Thr	Leu	Phe	Thr	Thr	Pro	Val	Ile	Tyr	Leu	Leu	Phe	Asp	Arg	1010	1015	1020
Leu	Ala	Leu	Trp	Thr	Lys	Ser	Arg	Phe	Ala	Arg	His	Glu	Glu	Glu	Ala	1025	1030	1035
																		1040

<210> 283  
 <211> 1025  
 <212> PRT  
 <213> E. Coli

<400> 283  
 Met Lys Phe Phe Ala Leu Phe Ile Tyr Arg Pro Val Ala Thr Ile Leu  
 1 5 10 15  
 Leu Ser Val Ala Ile Thr Leu Cys Gly Ile Leu Gly Phe Arg Met Leu  
 20 25 30  
 Pro Val Ala Pro Leu Pro Gln Val Asp Phe Pro Val Ile Ile Val Ser  
 35 40 45  
 Ala Ser Leu Pro Gly Ala Ser Pro Glu Thr Met Ala Ser Ser Val Ala  
 50 55 60  
 Thr Pro Leu Glu Arg Ser Leu Gly Arg Ile Ala Gly Val Ser Glu Met

65	Thr	Ser	Ser	Ser	Ser	Leu	Gly	Ser	Thr	Arg	Ile	Ile	Leu	Gln	Phe	Asp	80
					85					90						95	
Phe	Asp	Arg	Asp	Ile	Asn	Gly	Ala	Ala	Arg	Asp	Val	Gln	Ala	Ala	Ile		
			100					105						110			
Asn	Ala	Ala	Gln	Ser	Leu	Leu	Pro	Ser	Gly	Met	Pro	Ser	Arg	Pro	Thr		
			115					120						125			
Tyr	Arg	Lys	Ala	Asn	Pro	Ser	Asp	Ala	Pro	Ile	Met	Ile	Leu	Thr	Leu		
	130					135					140						
Thr	Ser	Asp	Thr	Tyr	Ser	Gln	Gly	Glu	Leu	Tyr	Asp	Phe	Ala	Ser	Thr		
	145				150					155					160		
Gln	Leu	Ala	Pro	Thr	Ile	Ser	Gln	Ile	Asp	Gly	Val	Gly	Asp	Val	Asp		
				165					170						175		
Val	Gly	Gly	Ser	Ser	Leu	Pro	Ala	Val	Arg	Val	Gly	Leu	Asn	Pro	Gln		
			180					185						190			
Ala	Leu	Phe	Asn	Gln	Gly	Val	Ser	Leu	Asp	Asp	Val	Arg	Thr	Ala	Val		
		195					200						205				
Ser	Asn	Ala	Asn	Val	Arg	Lys	Pro	Gln	Gly	Ala	Leu	Glu	Asp	Gly	Thr		
	210					215					220						
His	Arg	Trp	Gln	Ile	Gln	Thr	Asn	Asp	Glu	Leu	Lys	Thr	Ala	Ala	Glu		
	225				230				235						240		
Tyr	Gln	Pro	Leu	Ile	Ile	His	Tyr	Asn	Asn	Gly	Gly	Ala	Val	Arg	Leu		
				245					250						255		
Gly	Asp	Val	Ala	Thr	Val	Thr	Asp	Ser	Val	Gln	Asp	Val	Arg	Asn	Ala		
		260						265						270			
Gly	Met	Thr	Asn	Ala	Lys	Pro	Ala	Ile	Leu	Leu	Met	Ile	Arg	Lys	Leu		
	275						280					285					
Pro	Glu	Ala	Asn	Ile	Ile	Gln	Thr	Val	Asp	Ser	Ile	Arg	Ala	Lys	Leu		
	290					295					300						
Pro	Glu	Leu	Gln	Glu	Thr	Ile	Pro	Ala	Ala	Ile	Asp	Leu	Gln	Ile	Ala		
	305				310					315					320		
Gln	Asp	Arg	Ser	Pro	Thr	Ile	Arg	Ala	Ser	Leu	Glu	Glu	Val	Glu	Gln		
				325					330						335		
Thr	Leu	Ile	Ile	Ser	Val	Ala	Leu	Val	Ile	Leu	Val	Val	Phe	Leu	Phe		
				340				345					350				
Leu	Arg	Ser	Gly	Arg	Ala	Thr	Ile	Ile	Pro	Ala	Val	Ser	Val	Pro	Val		
	355					360						365					
Ser	Leu	Ile	Gly	Thr	Phe	Ala	Ala	Met	Tyr	Leu	Cys	Gly	Phe	Ser	Leu		
	370				375						380						
Asn	Asn	Leu	Ser	Leu	Met	Ala	Leu	Thr	Ile	Ala	Thr	Gly	Phe	Val	Val		
	385				390					395					400		
Asp	Asp	Ala	Ile	Val	Val	Leu	Glu	Asn	Ile	Ala	Arg	His	Leu	Glu	Ala		
				405					410					415			
Gly	Met	Lys	Pro	Leu	Gln	Ala	Ala	Leu	Gln	Gly	Thr	Arg	Glu	Val	Gly		
			420					425					430				
Phe	Thr	Val	Leu	Ser	Met	Ser	Leu	Ser	Leu	Val	Ala	Val	Phe	Leu	Pro		
	435						440					445					
Leu	Leu	Leu	Met	Gly	Gly	Leu	Pro	Gly	Arg	Leu	Leu	Arg	Glu	Phe	Ala		
	450					455					460						
Val	Thr	Leu	Ser	Val	Ala	Ile	Gly	Ile	Ser	Leu	Leu	Val	Ser	Leu	Thr		
	465				470				475						480		
Leu	Thr	Pro	Met	Met	Cys	Gly	Trp	Met	Leu	Lys	Ala	Ser	Lys	Pro	Arg		
				485					490					495			
Glu	Gln	Lys	Arg	Leu	Arg	Gly	Phe	Gly	Arg	Met	Leu	Val	Ala	Leu	Gln		
			500					505					510				
Gln	Gly	Tyr	Gly	Lys	Ser	Leu	Lys	Trp	Val	Leu	Asn	His	Thr	Arg	Leu		
	515						520					525					
Val	Gly	Val	Val	Leu	Leu	Gly	Thr	Ile	Ala	Leu	Asn	Ile	Trp	Leu	Tyr		
	530					535					540						
Ile	Ser	Ile	Pro	Lys	Thr	Phe	Phe	Pro	Glu	Gln	Asp	Thr	Gly	Val	Leu		
	545				550					555					560		

Met Gly Gly Ile Gln Ala Asp Gln Ser Ile Ser Phe Gln Ala Met Arg  
 565 570 575  
 Gly Lys Leu Gln Asp Phe Met Lys Ile Ile Arg Asp Asp Pro Ala Val  
 580 585 590  
 Asp Asn Val Thr Gly Phe Thr Gly Gly Ser Arg Val Asn Ser Gly Met  
 595 600 605  
 Met Phe Ile Thr Leu Lys Pro Arg Asp Glu Arg Ser Glu Thr Ala Gln  
 610 615 620  
 Gln Ile Ile Asp Arg Leu Arg Val Lys Leu Ala Lys Glu Pro Gly Ala  
 625 630 635 640  
 Asn Leu Phe Leu Met Ala Val Gln Asp Ile Arg Val Gly Gly Arg Gln  
 645 650 655  
 Ser Asn Ala Ser Tyr Gln Tyr Thr Leu Leu Ser Asp Asp Leu Ala Ala  
 660 665 670  
 Leu Arg Glu Trp Glu Pro Lys Ile Arg Lys Lys Leu Ala Thr Leu Pro  
 675 680 685  
 Glu Leu Ala Asp Val Asn Ser Asp Gln Gln Asp Asn Gly Ala Glu Met  
 690 695 700  
 Asn Leu Val Tyr Asp Arg Asp Thr Met Ala Arg Leu Gly Ile Asp Val  
 705 710 715 720  
 Gln Ala Ala Asn Ser Leu Leu Asn Asn Ala Phe Gly Gln Arg Gln Ile  
 725 730 735  
 Ser Thr Ile Tyr Gln Pro Met Asn Gln Tyr Lys Val Val Met Glu Val  
 740 745 750  
 Asp Pro Arg Tyr Thr Gln Asp Ile Ser Ala Leu Glu Lys Met Phe Val  
 755 760 765  
 Ile Asn Asn Glu Gly Lys Ala Ile Pro Leu Ser Tyr Phe Ala Lys Trp  
 770 775 780  
 Gln Pro Ala Asn Ala Pro Leu Ser Val Asn His Gln Gly Leu Ser Ala  
 785 790 795 800  
 Ala Ser Thr Ile Ser Phe Asn Leu Pro Thr Gly Lys Ser Leu Ser Asp  
 805 810 815  
 Ala Ser Ala Ala Ile Asp Arg Ala Met Thr Gln Leu Gly Val Pro Ser  
 820 825 830  
 Thr Val Arg Gly Ser Phe Ala Gly Thr Ala Gln Val Phe Gln Glu Thr  
 835 840 845  
 Met Asn Ser Gln Val Ile Leu Ile Ala Ala Ile Ala Thr Val Tyr  
 850 855 860  
 Ile Val Leu Gly Ile Leu Tyr Glu Ser Tyr Val His Pro Leu Thr Ile  
 865 870 875 880  
 Leu Ser Thr Leu Pro Ser Ala Gly Val Gly Ala Leu Leu Ala Leu Glu  
 885 890 895  
 Leu Phe Asn Ala Pro Phe Ser Leu Ile Ala Leu Ile Gly Ile Met Leu  
 900 905 910  
 Leu Ile Gly Ile Val Lys Lys Asn Ala Ile Met Met Val Asp Phe Ala  
 915 920 925  
 Leu Glu Ala Gln Arg His Gly Asn Leu Thr Pro Gln Glu Ala Ile Phe  
 930 935 940  
 Gln Ala Cys Leu Leu Arg Phe Arg Pro Ile Met Met Thr Thr Leu Ala  
 945 950 955 960  
 Ala Leu Phe Gly Ala Leu Pro Leu Val Leu Ser Gly Gly Asp Gly Ser  
 965 970 975  
 Glu Leu Arg Gln Pro Leu Gly Ile Thr Ile Val Gly Gly Leu Val Met  
 980 985 990  
 Ser Gln Leu Thr Leu Tyr Thr Thr Pro Val Val Tyr Leu Phe Phe  
 995 1000 1005  
 Asp Arg Leu Arg Leu Arg Phe Ser Arg Lys Pro Lys Gln Thr Val Thr  
 1010 1015 1020  
 Glu  
 1025



<210> 284  
 <211> 471  
 <212> PRT  
 <213> E. Coli

<400> 284  
 Met Thr Asp Leu Pro Asp Ser Thr Arg Trp Gln Leu Trp Ile Val Ala  
 1 5 10 15  
 Phe Gly Phe Phe Met Gln Ser Leu Asp Thr Thr Ile Val Asn Thr Ala  
 20 25 30  
 Leu Pro Ser Met Ala Gln Ser Leu Gly Glu Ser Pro Leu His Met His  
 35 40 45  
 Met Val Ile Val Ser Tyr Val Leu Thr Val Ala Val Met Leu Pro Ala  
 50 55 60  
 Ser Gly Trp Leu Ala Asp Lys Val Gly Val Arg Asn Ile Phe Phe Thr  
 65 70 75 80  
 Ala Ile Val Leu Phe Thr Leu Gly Ser Leu Phe Cys Ala Leu Ser Gly  
 85 90 95  
 Thr Leu Asn Glu Leu Leu Leu Ala Arg Ala Leu Gln Gly Val Gly Gly  
 100 105 110  
 Ala Met Met Val Pro Val Gly Arg Leu Thr Val Met Lys Ile Val Pro  
 115 120 125  
 Arg Glu Gln Tyr Met Ala Ala Met Thr Phe Val Thr Leu Pro Gly Gln  
 130 135 140  
 Val Gly Pro Leu Leu Gly Pro Ala Leu Gly Gly Leu Leu Val Glu Tyr  
 145 150 155 160  
 Ala Ser Trp His Trp Ile Phe Leu Ile Asn Ile Pro Val Gly Ile Ile  
 165 170 175  
 Gly Ala Ile Ala Thr Leu Leu Leu Met Pro Asn Tyr Thr Met Gln Thr  
 180 185 190  
 Arg Arg Phe Asp Leu Ser Gly Phe Leu Leu Leu Ala Val Gly Met Ala  
 195 200 205  
 Val Leu Thr Leu Ala Leu Asp Gly Ser Lys Gly Thr Gly Leu Ser Pro  
 210 215 220  
 Leu Thr Ile Ala Gly Leu Val Ala Val Gly Val Val Ala Leu Val Leu  
 225 230 235 240  
 Tyr Leu Leu His Ala Arg Asn Asn Asn Arg Ala Leu Phe Ser Leu Lys  
 245 250 255  
 Leu Phe Arg Thr Arg Thr Phe Ser Leu Gly Leu Ala Gly Ser Phe Ala  
 260 265 270  
 Gly Arg Ile Gly Ser Gly Met Leu Pro Phe Met Thr Pro Val Phe Leu  
 275 280 285  
 Gln Ile Gly Leu Gly Phe Ser Pro Phe His Ala Gly Leu Met Met Ile  
 290 295 300  
 Pro Met Val Leu Gly Ser Met Gly Met Lys Arg Ile Val Val Gln Val  
 305 310 315 320  
 Val Asn Arg Phe Gly Tyr Arg Arg Val Leu Val Ala Thr Thr Leu Gly  
 325 330 335  
 Leu Ser Leu Val Thr Leu Leu Phe Met Thr Thr Ala Leu Leu Gly Trp  
 340 345 350  
 Tyr Tyr Val Leu Pro Phe Val Leu Phe Leu Gln Gly Met Val Asn Ser  
 355 360 365  
 Thr Arg Phe Ser Ser Met Asn Thr Leu Thr Leu Lys Asp Leu Pro Asp  
 370 375 380  
 Asn Leu Ala Ser Ser Gly Asn Ser Leu Leu Ser Met Ile Met Gln Leu  
 385 390 395 400  
 Ser Met Ser Ile Gly Val Thr Ile Ala Gly Leu Leu Leu Gly Leu Phe  
 405 410 415  
 Gly Ser Gln His Val Ser Val Asp Ser Gly Thr Thr Gln Thr Val Phe  
 420 425 430

Met Tyr Thr Trp Leu Ser Met Ala Leu Ile Ile Ala Leu Pro Ala Phe  
 435 440 445  
 Ile Phe Ala Arg Val Pro Asn Asp Thr His Gln Asn Val Ala Ile Ser  
 450 455 460  
 Arg Arg Lys Arg Ser Ala Gln  
 465 470

<210> 285  
 <211> 344  
 <212> PRT  
 <213> E. Coli

<400> 285  
 Met Glu Ile Arg Ile Met Leu Phe Ile Leu Met Met Met Val Met Pro  
 1 5 10 15  
 Val Ser Tyr Ala Ala Cys Tyr Ser Glu Leu Ser Val Gln His Asn Leu  
 20 25 30  
 Val Val Gln Gly Asp Phe Ala Leu Thr Gln Thr Gln Met Ala Thr Tyr  
 35 40 45  
 Glu His Asn Phe Asn Asp Ser Ser Cys Val Ser Thr Asn Thr Ile Thr  
 50 55 60  
 Pro Met Ser Pro Ser Asp Ile Ile Val Gly Leu Tyr Asn Asp Thr Ile  
 65 70 75 80  
 Lys Leu Asn Leu His Phe Glu Trp Thr Asn Lys Asn Asn Ile Thr Leu  
 85 90 95  
 Ser Asn Asn Gln Thr Ser Phe Thr Ser Gly Tyr Ser Val Thr Val Thr  
 100 105 110  
 Pro Ala Ala Ser Asn Ala Lys Val Asn Val Ser Ala Gly Gly Gly Gly  
 115 120 125  
 Ser Val Met Ile Asn Gly Val Ala Thr Leu Ser Ser Ala Ser Ser Ser  
 130 135 140  
 Thr Arg Gly Ser Ala Ala Val Gln Phe Leu Leu Cys Leu Leu Gly Gly  
 145 150 155 160  
 Lys Ser Trp Asp Ala Cys Val Asn Ser Tyr Arg Asn Ala Leu Ala Gln  
 165 170 175  
 Asn Ala Gly Val Tyr Ser Phe Asn Leu Thr Leu Ser Tyr Asn Pro Ile  
 180 185 190  
 Thr Thr Thr Cys Lys Pro Asp Asp Leu Leu Ile Thr Leu Asp Ser Ile  
 195 200 205  
 Pro Val Ser Gln Leu Pro Ala Thr Gly Asn Lys Ala Thr Ile Asn Ser  
 210 215 220  
 Lys Gln Gly Asp Ile Ile Leu Arg Cys Lys Asn Leu Leu Gly Gln Gln  
 225 230 235 240  
 Asn Gln Thr Ser Arg Lys Met Gln Val Tyr Leu Ser Ser Ser Asp Leu  
 245 250 255  
 Leu Thr Asn Ser Asn Thr Ile Leu Lys Gly Ala Glu Asp Asn Gly Val  
 260 265 270  
 Gly Phe Ile Leu Glu Ser Asn Gly Ser Pro Val Thr Leu Leu Asn Ile  
 275 280 285  
 Thr Asn Ser Ser Lys Gly Tyr Thr Asn Leu Lys Glu Val Ala Ala Lys  
 290 295 300  
 Ser Lys Leu Thr Asp Thr Thr Val Ser Ile Pro Ile Thr Ala Ser Tyr  
 305 310 315 320  
 Tyr Val Tyr Asp Thr Asn Lys Val Lys Ser Gly Ala Leu Glu Ala Thr  
 325 330 335  
 Ala Leu Ile Asn Val Lys Tyr Asp  
 340

<210> 286

<211> 826  
 <212> PRT  
 <213> E. Coli

<400> 286

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Met Leu Arg Met Thr Pro Leu Ala Ser Ala Ile Val Ala Leu Leu Leu
 1          5          10          15
Gly Ile Glu Ala Tyr Ala Ala Glu Glu Thr Phe Asp Thr His Phe Met
 20          25          30
Ile Gly Gly Met Lys Asp Gln Gln Val Ala Asn Ile Arg Leu Asp Asp
 35          40          45
Asn Gln Pro Leu Pro Gly Gln Tyr Asp Ile Asp Ile Tyr Val Asn Lys
 50          55          60
Gln Trp Arg Gly Lys Tyr Glu Ile Ile Val Lys Asp Asn Pro Gln Glu
 65          70          75          80
Thr Cys Leu Ser Arg Glu Val Ile Lys Arg Leu Gly Ile Asn Ser Asp
 85          90          95
Asn Phe Ala Ser Gly Lys Gln Cys Leu Thr Phe Glu Gln Leu Val Gln
100          105          110
Gly Gly Ser Tyr Thr Trp Asp Ile Gly Val Phe Arg Leu Asp Phe Ser
115          120          125
Val Pro Gln Ala Trp Val Glu Glu Leu Glu Ser Gly Tyr Val Pro Pro
130          135          140
Glu Asn Trp Glu Arg Gly Ile Asn Ala Phe Tyr Thr Ser Tyr Tyr Leu
145          150          155          160
Ser Gln Tyr Tyr Ser Asp Tyr Lys Ala Ser Gly Asn Asn Lys Ser Thr
165          170          175
Tyr Val Arg Phe Asn Ser Gly Leu Asn Leu Leu Gly Trp Gln Leu His
180          185          190
Ser Asp Ala Ser Phe Ser Lys Thr Asn Asn Asn Pro Gly Val Trp Lys
195          200          205
Ser Asn Thr Leu Tyr Leu Glu Arg Gly Phe Ala Gln Leu Leu Gly Thr
210          215          220
Leu Arg Val Gly Asp Met Tyr Thr Ser Ser Asp Ile Phe Asp Ser Val
225          230          235          240
Arg Phe Arg Gly Val Arg Leu Phe Arg Asp Met Gln Met Leu Pro Asn
245          250          255
Ser Lys Gln Asn Phe Thr Pro Arg Val Gln Gly Ile Ala Gln Ser Asn
260          265          270
Ala Leu Val Thr Ile Glu Gln Asn Gly Phe Val Val Tyr Gln Lys Glu
275          280          285
Val Pro Pro Gly Pro Phe Ala Ile Thr Asp Leu Gln Leu Ala Gly Gly
290          295          300
Gly Ala Asp Leu Asp Val Ser Val Lys Glu Ala Asp Gly Ser Val Thr
305          310          315          320
Thr Tyr Leu Val Pro Tyr Ala Ala Val Pro Asn Met Leu Gln Pro Gly
325          330          335
Val Ser Lys Tyr Asp Leu Ala Ala Gly Arg Ser His Ile Glu Gly Ala
340          345          350
Ser Lys Gln Ser Asp Phe Val Gln Ala Gly Tyr Gln Tyr Gly Phe Asn
355          360          365
Asn Leu Leu Thr Leu Tyr Gly Gly Ser Met Val Ala Asn Asn Tyr Tyr
370          375          380
Ala Phe Thr Leu Gly Ala Gly Trp Asn Thr Arg Ile Gly Ala Ile Ser
385          390          395          400
Val Asp Ala Thr Lys Ser His Ser Lys Gln Asp Asn Gly Asp Val Phe
405          410          415
Asp Gly Gln Ser Tyr Gln Ile Ala Tyr Asn Lys Phe Val Ser Gln Thr
420          425          430
Ser Thr Arg Phe Gly Leu Ala Ala Trp Arg Tyr Ser Ser Arg Asp Tyr
435          440          445

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Arg Thr Phe Asn Asp His Val Trp Ala Asn Asn Lys Asp Asn Tyr Arg  
 450 455 460  
 Arg Asp Glu Asn Asp Val Tyr Asp Ile Ala Asp Tyr Tyr Gln Asn Asp  
 465 470 475 480  
 Phe Gly Arg Lys Asn Ser Phe Ser Ala Asn Met Ser Gln Ser Leu Ser Pro  
 485 490 495  
 Glu Gly Trp Gly Ser Val Ser Leu Ser Thr Leu Trp Arg Asp Tyr Trp  
 500 505 510  
 Gly Arg Ser Gly Ser Ser Lys Asp Tyr Gln Leu Ser Tyr Ser Asn Asn  
 515 520 525  
 Leu Arg Arg Ile Ser Tyr Thr Leu Ala Ala Ser Gln Ala Tyr Asp Glu  
 530 535 540  
 Asn His His Glu Glu Lys Arg Phe Asn Ile Phe Ile Ser Ile Pro Phe  
 545 550 555 560  
 Asp Trp Gly Asp Asp Val Ser Thr Pro Arg Arg Gln Ile Tyr Met Ser  
 565 570 575  
 Asn Ser Thr Thr Phe Asp Asp Gln Gly Phe Ala Ser Asn Asn Thr Gly  
 580 585 590  
 Leu Ser Gly Thr Val Gly Ser Arg Asp Gln Phe Asn Tyr Gly Val Asn  
 595 600 605  
 Leu Ser His Gln His Gln Gly Asn Glu Thr Thr Ala Gly Ala Asn Leu  
 610 615 620  
 Thr Trp Asn Ala Pro Val Ala Thr Val Asn Gly Ser Tyr Ser Gln Ser  
 625 630 635 640  
 Ser Thr Tyr Arg Gln Ala Gly Ala Ser Val Ser Gly Gly Ile Val Ala  
 645 650 655  
 Trp Ser Gly Gly Val Asn Leu Ala Asn Arg Leu Ser Glu Thr Phe Ala  
 660 665 670  
 Val Met Asn Ala Pro Gly Ile Lys Asp Ala Tyr Val Asn Gly Gln Lys  
 675 680 685  
 Tyr Arg Thr Thr Asn Arg Asn Gly Val Val Ile Tyr Asp Gly Met Thr  
 690 695 700  
 Pro Tyr Arg Glu Asn His Leu Met Leu Asp Val Ser Gln Ser Asp Ser  
 705 710 715 720  
 Glu Ala Glu Leu Arg Gly Asn Arg Lys Ile Ala Ala Pro Tyr Arg Gly  
 725 730 735  
 Ala Val Val Leu Val Asn Phe Asp Thr Asp Gln Arg Lys Pro Trp Phe  
 740 745 750  
 Ile Lys Ala Leu Arg Ala Asp Gly Gln Ser Leu Thr Phe Gly Tyr Glu  
 755 760 765  
 Val Asn Asp Ile His Gly His Asn Ile Gly Val Val Gly Gln Gly Ser  
 770 775 780  
 Gln Leu Phe Ile Arg Thr Asn Glu Val Pro Pro Ser Val Asn Val Ala  
 785 790 795 800  
 Ile Asp Lys Gln Gln Gly Leu Ser Cys Thr Ile Thr Phe Gly Lys Glu  
 805 810 815  
 Ile Asp Glu Ser Arg Asn Tyr Ile Cys Gln  
 820 825

&lt;210&gt; 287

&lt;211&gt; 239

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 287

Met Ala Ala Ile Pro Trp Arg Pro Phe Asn Leu Arg Gly Ile Lys Met  
 1 5 10 15  
 Lys Gly Leu Leu Ser Leu Leu Ile Phe Ser Met Val Leu Pro Ala His  
 20 25 30  
 Ala Gly Ile Val Ile Tyr Gly Thr Arg Ile Ile Tyr Pro Ala Glu Asn

35	40	45
Lys Glu Val Met Val Gln Leu Met Asn Gln Gly Asn Arg Ser Ser Leu		
50	55	60
Leu Gln Ala Trp Ile Asp Asp Gly Asp Thr Ser Leu Pro Pro Glu Lys		
65	70	75
Ile Gln Val Pro Phe Met Leu Thr Pro Pro Val Ala Lys Ile Gly Ala		
85	90	95
Asn Ser Gly Gln Val Lys Ile Lys Ile Met Pro Asn Lys Leu Pro		
100	105	110
Thr Asn Lys Glu Ser Ile Phe Tyr Leu Asn Val Leu Asp Ile Pro Pro		
115	120	125
Asn Ser Pro Glu Gln Glu Gly Lys Asn Ala Leu Lys Phe Ala Met Gln		
130	135	140
Asn Arg Ile Lys Leu Phe Tyr Arg Pro Ala Gly Ile Ala Pro Val Asn		
145	150	155
Lys Ala Thr Phe Lys Lys Leu Leu Val Asn Arg Ser Gly Asn Gly Leu		
165	170	175
Val Ile Lys Asn Asp Ser Ala Asn Trp Val Thr Ile Ser Asp Val Lys		
180	185	190
Ala Asn Asn Val Lys Val Asn Tyr Glu Thr Ile Met Ile Ala Pro Leu		
195	200	205
Glu Ser Gln Ser Val Asn Val Lys Ser Asn Asn Ala Asn Asn Trp His		
210	215	220
Leu Thr Ile Ile Asp Asp His Gly Asn Tyr Ile Ser Asp Lys Ile		
225	230	235

&lt;210&gt; 288

&lt;211&gt; 180

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 288

Met Lys Arg Ser Ile Ile Ala Ala Ala Val Phe Ser Ser Phe Phe Met	
1	5
Ser Ala Gly Val Phe Ala Ala Asp Val Asp Thr Gly Thr Leu Thr Ile	
20	25
Lys Gly Asn Ile Ala Glu Ser Pro Cys Lys Phe Glu Ala Gly Gly Asp	
35	40
Ser Val Ser Ile Asn Met Pro Thr Val Pro Thr Ser Val Phe Glu Gly	
50	55
Lys Ala Lys Tyr Ser Thr Tyr Asp Asp Ala Val Gly Val Thr Ser Ser	
65	70
Met Leu Lys Ile Ser Cys Pro Lys Glu Val Ala Gly Val Lys Leu Ser	
85	90
Leu Ile Thr Asn Asp Lys Ile Thr Gly Asn Asp Lys Ala Ile Ala Ser	
100	105
Ser Asn Asp Thr Val Gly Tyr Tyr Leu Tyr Leu Gly Asp Asn Ser Asp	
115	120
Val Leu Asp Val Ser Ala Pro Phe Asn Ile Glu Ser Tyr Lys Thr Ala	
130	135
Glu Gly Gln Tyr Ala Ile Pro Phe Lys Ala Lys Tyr Leu Lys Leu Thr	
145	150
Asp Asn Ser Val Gln Ser Gly Asp Val Leu Ser Ser Leu Val Met Arg	
165	170
Val Ala Gln Asp	
180	

&lt;210&gt; 289

<211> 112  
 <212> PRT  
 <213> E. Coli

<400> 289  
 Met Ser Ser Glu Arg Asp Leu Val Asn Phe Leu Gly Asp Phe Ser Met  
 1 5 10 15  
 Asp Val Ala Lys Ala Val Ile Ala Gly Gly Val Ala Thr Ala Ile Gly  
 20 25 30  
 Ser Leu Ala Ser Phe Ala Cys Val Ser Phe Gly Phe Pro Val Ile Leu  
 35 40 45  
 Val Gly Gly Ala Ile Leu Leu Thr Gly Ile Val Cys Thr Val Val Leu  
 50 55 60  
 Asn Glu Ile Asp Ala Gln Cys His Leu Ser Glu Lys Leu Lys Tyr Ala  
 65 70 75 80  
 Ile Arg Asp Gly Leu Lys Arg Gln Gln Glu Leu Asp Lys Trp Lys Arg  
 85 90 95  
 Glu Asn Met Thr Pro Phe Met Tyr Val Leu Asn Thr Pro Pro Val Ile  
 100 105 110

<210> 290  
 <211> 193  
 <212> PRT  
 <213> E. Coli

<400> 290  
 Met Thr Asp Tyr Leu Leu Leu Phe Val Gly Thr Val Leu Val Asn Asn  
 1 5 10 15  
 Phe Val Leu Val Lys Phe Leu Gly Leu Cys Pro Phe Met Gly Val Ser  
 20 25 30  
 Lys Lys Leu Glu Thr Ala Met Gly Met Gly Leu Ala Thr Thr Phe Val  
 35 40 45  
 Met Thr Leu Ala Ser Ile Cys Ala Trp Leu Ile Asp Thr Trp Ile Leu  
 50 55 60  
 Ile Pro Leu Asn Leu Ile Tyr Leu Arg Thr Leu Ala Phe Ile Leu Val  
 65 70 75 80  
 Ile Ala Val Val Val Gln Phe Thr Glu Met Val Val Arg Lys Thr Ser  
 85 90 95  
 Pro Val Leu Tyr Arg Leu Leu Gly Ile Phe Leu Pro Leu Ile Thr Thr  
 100 105 110  
 Asn Cys Ala Val Leu Gly Val Ala Leu Leu Asn Ile Asn Leu Gly His  
 115 120 125  
 Asn Phe Leu Gln Ser Ala Leu Tyr Gly Phe Ser Ala Ala Val Gly Phe  
 130 135 140  
 Ser Leu Val Met Val Leu Phe Ala Ala Ile Arg Glu Arg Leu Ala Val  
 145 150 155 160  
 Ala Asp Val Pro Ala Pro Phe Arg Gly Asn Ala Ile Ala Leu Ile Thr  
 165 170 175  
 Ala Gly Leu Met Ser Leu Ala Phe Met Gly Phe Ser Gly Leu Val Lys  
 180 185 190  
 Leu

<210> 291  
 <211> 192  
 <212> PRT  
 <213> E. Coli

&lt;400&gt; 291

Met Asn Ala Ile Trp Ile Ala Val Ala Ala Val Ser Leu Leu Gly Leu  
 1 5 10 15  
 Ala Phe Gly Ala Ile Leu Gly Tyr Ala Ser Arg Arg Phe Ala Val Glu  
 20 25 30  
 Asp Asp Pro Val Val Glu Lys Ile Asp Glu Ile Leu Pro Gln Ser Gln  
 35 40 45  
 Cys Gly Gln Cys Gly Tyr Pro Gly Cys Arg Pro Tyr Ala Glu Ala Ile  
 50 55 60  
 Ser Cys Asn Gly Glu Lys Ile Asn Arg Cys Ala Pro Gly Gly Glu Ala  
 65 70 75 80  
 Val Met Leu Lys Ile Ala Glu Leu Leu Asn Val Glu Pro Gln Pro Leu  
 85 90 95  
 Asp Gly Glu Ala Gln Glu Ile Thr Pro Ala Arg Met Val Ala Val Ile  
 100 105 110  
 Asp Glu Asn Asn Cys Ile Gly Cys Thr Lys Cys Ile Gln Ala Cys Pro  
 115 120 125  
 Val Asp Ala Ile Val Gly Ala Thr Arg Ala Met His Thr Val Met Ser  
 130 135 140  
 Asp Leu Cys Thr Gly Cys Asn Leu Cys Val Asp Pro Cys Pro Thr His  
 145 150 155 160  
 Cys Ile Ser Leu Gln Pro Val Ala Glu Thr Pro Asp Ser Trp Lys Trp  
 165 170 175  
 Asp Leu Asn Thr Ile Pro Val Arg Ile Ile Pro Val Glu His His Ala  
 180 185 190

&lt;210&gt; 292

&lt;211&gt; 740

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 292

Met Leu Lys Leu Phe Ser Ala Phe Arg Lys Asn Lys Ile Trp Asp Phe  
 1 5 10 15  
 Asn Gly Gly Ile His Pro Pro Glu Met Lys Thr Gln Ser Asn Gly Thr  
 20 25 30  
 Pro Leu Arg Gln Val Pro Leu Ala Gln Arg Phe Val Ile Pro Leu Lys  
 35 40 45  
 Gln His Ile Gly Ala Glu Gly Glu Leu Cys Val Ser Val Gly Asp Lys  
 50 55 60  
 Val Leu Arg Gly Gln Pro Leu Thr Arg Gly Arg Gly Lys Met Leu Pro  
 65 70 75 80  
 Val His Ala Pro Thr Ser Gly Thr Val Thr Ala Ile Ala Pro His Ser  
 85 90 95  
 Thr Ala His Pro Ser Ala Leu Ala Glu Leu Ser Val Ile Ile Asp Ala  
 100 105 110  
 Asp Gly Glu Asp Cys Trp Ile Pro Arg Asp Gly Trp Ala Asp Tyr Arg  
 115 120 125  
 Thr Arg Ser Arg Glu Glu Leu Ile Glu Arg Ile His Gln Phe Gly Val  
 130 135 140  
 Ala Gly Leu Gly Gly Ala Gly Phe Pro Thr Gly Val Lys Leu Gln Gly  
 145 150 155 160  
 Gly Gly Asp Lys Ile Glu Thr Leu Ile Ile Asn Ala Ala Glu Cys Glu  
 165 170 175  
 Pro Tyr Ile Thr Ala Asp Asp Arg Leu Met Gln Asp Cys Ala Ala Gln  
 180 185 190  
 Val Val Glu Gly Ile Arg Ile Leu Ala His Ile Leu Gln Pro Arg Glu  
 195 200 205  
 Ile Leu Ile Gly Ile Glu Asp Asn Lys Pro Gln Ala Ile Ser Met Leu  
 210 215 220

Arg	Ala	Val	Leu	Ala	Asp	Ser	Asn	Asp	Ile	Ser	Leu	Arg	Val	Ile	Pro
225					230					235					240
Thr	Lys	Tyr	Pro	Ser	Gly	Gly	Ala	Lys	Gln	Leu	Thr	Tyr	Ile	Leu	Thr
				245					250					255	
Gly	Lys	Gln	Val	Pro	His	Gly	Gly	Arg	Ser	Ser	Asp	Ile	Gly	Val	Leu
			260					265					270		
Met	Gln	Asn	Val	Gly	Thr	Ala	Tyr	Ala	Val	Lys	Arg	Ala	Val	Ile	Asp
		275					280					285			
Gly	Glu	Pro	Ile	Thr	Glu	Arg	Val	Val	Thr	Leu	Thr	Gly	Glu	Ala	Ile
	290					295					300				
Ala	Arg	Pro	Gly	Asn	Val	Trp	Ala	Arg	Leu	Gly	Thr	Pro	Val	Arg	His
305					310					315					320
Leu	Leu	Asn	Asp	Ala	Gly	Phe	Cys	Pro	Ser	Ala	Asp	Gln	Met	Val	Ile
				325					330					335	
Met	Gly	Gly	Pro	Leu	Met	Gly	Phe	Thr	Leu	Pro	Trp	Leu	Asp	Val	Pro
			340					345					350		
Val	Val	Lys	Ile	Thr	Asn	Cys	Leu	Leu	Ala	Pro	Ser	Ala	Asn	Glu	Leu
		355					360					365			
Gly	Glu	Pro	Gln	Glu	Glu	Gln	Ser	Cys	Ile	Arg	Cys	Ser	Ala	Cys	Ala
	370					375					380				
Asp	Ala	Cys	Pro	Ala	Asp	Leu	Leu	Pro	Gln	Gln	Leu	Tyr	Trp	Phe	Ser
385					390					395					400
Lys	Gly	Gln	Gln	His	Asp	Lys	Ala	Thr	Thr	His	Asn	Ile	Ala	Asp	Cys
				405					410					415	
Ile	Glu	Cys	Gly	Ala	Cys	Ala	Trp	Val	Cys	Pro	Ser	Asn	Ile	Pro	Leu
			420					425					430		
Val	Gln	Tyr	Phe	Arg	Gln	Glu	Lys	Ala	Glu	Ile	Ala	Ala	Ile	Arg	Gln
		435					440					445			
Glu	Glu	Lys	Arg	Ala	Ala	Glu	Ala	Lys	Ala	Arg	Phe	Glu	Ala	Arg	Gln
	450					455					460				
Ala	Arg	Leu	Glu	Arg	Glu	Lys	Ala	Ala	Arg	Leu	Glu	Arg	His	Lys	Ser
465					470					475					480
Ala	Ala	Val	Gln	Pro	Ala	Ala	Lys	Asp	Lys	Asp	Ala	Ile	Ala	Ala	Ala
			485						490					495	
Leu	Ala	Arg	Val	Lys	Glu	Lys	Gln	Ala	Gln	Ala	Thr	Gln	Pro	Ile	Val
			500					505					510		
Ile	Lys	Ala	Gly	Glu	Arg	Pro	Asp	Asn	Ser	Ala	Ile	Ile	Ala	Ala	Arg
		515					520					525			
Glu	Ala	Arg	Lys	Ala	Gln	Ala	Arg	Ala	Lys	Gln	Ala	Glu	Leu	Gln	Gln
	530					535					540				
Thr	Asn	Asp	Ala	Ala	Thr	Val	Ala	Asp	Pro	Arg	Lys	Thr	Ala	Val	Glu
545					550					555					560
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
			565						570					575	
Asn	Ala	Glu	Pro	Glu	Gln	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
		580						585					590		
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
		595					600					605			
Asn	Ala	Glu	Pro	Glu	Glu	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
	610					615					620				
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
625					630					635					640
Asn	Ala	Glu	Pro	Glu	Gln	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
			645						650					655	
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Arg	Glu	Gln	Gln	Pro	Ala
		660						665				670			
Asn	Ala	Glu	Pro	Glu	Glu	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
		675					680					685			
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
	690					695					700				
Asn	Ala	Val	Pro	Glu	Glu	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Ala



705		710		715		720									
Ala	Ala	Ile	Ala	Arg	Ala	Gln	Ala	Lys	Lys	Ala	Ala	Gln	Gln	Lys	Val
				725					730					735	
Val	Asn	Glu	Asp												
			740												

<210> 293  
 <211> 352  
 <212> PRT  
 <213> E. Coli

<400> 293

Met	Val	Phe	Arg	Ile	Ala	Ser	Ser	Pro	Tyr	Thr	His	Asn	Gln	Arg	Gln
1				5					10					15	
Thr	Ser	Arg	Ile	Met	Leu	Leu	Val	Leu	Leu	Ala	Ala	Val	Pro	Gly	Ile
			20					25					30		
Ala	Ala	Gln	Leu	Trp	Phe	Phe	Gly	Trp	Gly	Thr	Leu	Val	Gln	Ile	Leu
		35					40					45			
Leu	Ala	Ser	Val	Ser	Ala	Leu	Leu	Ala	Glu	Ala	Leu	Val	Leu	Lys	Leu
	50					55					60				
Arg	Lys	Gln	Ser	Val	Ala	Thr	Leu	Lys	Asp	Asn	Ser	Ala	Leu	Leu	
65				70					75					80	
Thr	Gly	Leu	Leu	Leu	Ala	Val	Ser	Ile	Pro	Pro	Leu	Ala	Pro	Trp	Trp
				85					90					95	
Met	Val	Val	Leu	Gly	Thr	Val	Phe	Ala	Val	Ile	Ile	Ala	Lys	Gln	Leu
			100					105					110		
Tyr	Gly	Gly	Leu	Gly	Gln	Asn	Pro	Phe	Asn	Pro	Ala	Met	Ile	Gly	Tyr
		115					120					125			
Val	Val	Leu	Leu	Ile	Ser	Phe	Pro	Val	Gln	Met	Thr	Ser	Trp	Leu	Pro
	130					135					140				
Pro	His	Glu	Ile	Ala	Val	Asn	Ile	Pro	Gly	Phe	Ile	Asp	Ala	Ile	Gln
145					150					155					160
Val	Ile	Phe	Ser	Gly	His	Thr	Ala	Ser	Gly	Gly	Asp	Met	Asn	Thr	Leu
				165					170					175	
Arg	Leu	Gly	Ile	Asp	Gly	Ile	Ser	Gln	Ala	Thr	Pro	Leu	Asp	Thr	Phe
			180					185					190		
Lys	Thr	Ser	Val	Arg	Ala	Gly	His	Ser	Val	Glu	Gln	Ile	Met	Gln	Tyr
		195					200					205			
Pro	Ile	Tyr	Ser	Gly	Ile	Leu	Ala	Gly	Ala	Gly	Trp	Gln	Trp	Val	Asn
	210					215					220				
Leu	Ala	Trp	Leu	Ala	Gly	Gly	Val	Trp	Leu	Leu	Trp	Gln	Lys	Ala	Ile
225					230					235					240
Arg	Trp	His	Ile	Pro	Leu	Ser	Phe	Leu	Val	Thr	Leu	Ala	Leu	Cys	Ala
				245					250					255	
Met	Leu	Gly	Trp	Leu	Phe	Ser	Pro	Glu	Thr	Leu	Ala	Ala	Pro	Gln	Ile
			260					265					270		
His	Leu	Leu	Ser	Gly	Ala	Thr	Met	Leu	Gly	Ala	Phe	Phe	Ile	Leu	Thr
		275					280					285			
Asp	Pro	Val	Thr	Ala	Ser	Thr	Asn	Arg	Gly	Arg	Leu	Ile	Phe	Gly	
	290					295				300					
Ala	Leu	Ala	Gly	Leu	Leu	Val	Trp	Leu	Ile	Arg	Ser	Phe	Gly	Gly	Tyr
305					310				315						320
Pro	Asp	Gly	Val	Ala	Phe	Ala	Val	Leu	Leu	Ala	Asn	Ile	Thr	Val	Pro
				325					330					335	
Leu	Ile	Asp	Tyr	Tyr	Thr	Arg	Pro	Arg	Val	Tyr	Gly	His	Arg	Lys	Gly
			340					345					350		

<210> 294

<211> 206  
 <212> PRT  
 <213> E. Coli

<400> 294

Met	Leu	Lys	Thr	Ile	Arg	Lys	His	Gly	Ile	Thr	Leu	Ala	Leu	Phe	Ala
1				5					10					15	
Ala	Gly	Ser	Thr	Gly	Leu	Thr	Ala	Ala	Ile	Asn	Gln	Met	Thr	Lys	Thr
			20					25					30		
Thr	Ile	Ala	Glu	Gln	Ala	Ser	Leu	Gln	Gln	Lys	Ala	Leu	Phe	Asp	Gln
		35					40					45			
Val	Leu	Pro	Ala	Glu	Arg	Tyr	Asn	Asn	Ala	Leu	Ala	Gln	Ser	Cys	Tyr
	50					55				60					
Leu	Val	Thr	Ala	Pro	Glu	Leu	Gly	Lys	Gly	Glu	His	Arg	Val	Tyr	Ile
65					70				75						80
Ala	Lys	Gln	Asp	Asp	Lys	Pro	Val	Ala	Ala	Val	Leu	Glu	Ala	Thr	Ala
				85					90					95	
Pro	Asp	Gly	Tyr	Ser	Gly	Ala	Ile	Gln	Leu	Leu	Val	Gly	Ala	Asp	Phe
			100					105					110		
Asn	Gly	Thr	Val	Leu	Gly	Thr	Arg	Val	Thr	Glu	His	His	Glu	Thr	Pro
		115					120						125		
Gly	Leu	Gly	Asp	Lys	Ile	Glu	Leu	Arg	Leu	Ser	Asp	Trp	Ile	Thr	His
	130					135					140				
Phe	Ala	Gly	Lys	Lys	Ile	Ser	Gly	Ala	Asp	Asp	Ala	His	Trp	Ala	Val
145					150					155					160
Lys	Lys	Asp	Gly	Gly	Asp	Phe	Asp	Gln	Phe	Thr	Gly	Ala	Thr	Ile	Thr
				165					170					175	
Pro	Arg	Ala	Val	Val	Asn	Ala	Val	Lys	Arg	Ala	Gly	Leu	Tyr	Ala	Gln
			180					185						190	
Thr	Leu	Pro	Ala	Gln	Leu	Ser	Gln	Leu	Pro	Ala	Cys	Gly	Glu		
		195					200					205			

<210> 295  
 <211> 231  
 <212> PRT  
 <213> E. Coli

<400> 295

Met	Ser	Glu	Ile	Lys	Asp	Val	Ile	Val	Gln	Gly	Leu	Trp	Lys	Asn	Asn
1				5					10					15	
Ser	Ala	Leu	Val	Gln	Leu	Leu	Gly	Leu	Cys	Pro	Leu	Leu	Ala	Val	Thr
			20					25					30		
Ser	Thr	Ala	Thr	Asn	Ala	Leu	Gly	Leu	Gly	Leu	Ala	Thr	Thr	Leu	Val
		35					40					45			
Leu	Thr	Leu	Thr	Asn	Leu	Thr	Ile	Ser	Thr	Leu	Arg	His	Trp	Thr	Pro
	50					55				60					
Ala	Glu	Ile	Arg	Ile	Pro	Ile	Tyr	Val	Met	Ile	Ile	Ala	Ser	Val	Val
65					70					75					80
Ser	Ala	Val	Gln	Met	Leu	Ile	Asn	Ala	Tyr	Ala	Phe	Gly	Leu	Tyr	Gln
				85					90					95	
Ser	Leu	Gly	Ile	Phe	Ile	Pro	Leu	Ile	Val	Thr	Asn	Cys	Ile	Val	Val
			100					105					110		
Gly	Arg	Ala	Glu	Ala	Phe	Ala	Ala	Lys	Lys	Gly	Pro	Ala	Leu	Ser	Ala
		115					120					125			
Leu	Asp	Gly	Phe	Ser	Ile	Gly	Met	Gly	Ala	Thr	Cys	Ala	Met	Phe	Val
	130					135					140				
Leu	Gly	Ser	Leu	Arg	Glu	Ile	Ile	Gly	Asn	Gly	Thr	Leu	Phe	Asp	Gly
145					150					155					160
Ala	Asp	Ala	Leu	Leu	Gly	Ser	Trp	Ala	Lys	Val	Leu	Arg	Val	Glu	Ile
				165					170					175	

Phe His Thr Asp Ser Pro Phe Leu Leu Ala Met Leu Pro Pro Gly Ala  
 180 185 190  
 Phe Ile Gly Leu Gly Leu Met Leu Ala Gly Lys Tyr Leu Ile Asp Glu  
 195 200 205  
 Arg Met Lys Lys Arg Arg Ala Glu Ala Ala Ala Glu Arg Ala Leu Pro  
 210 215 220  
 Asn Gly Glu Thr Gly Asn Val  
 225 230

<210> 296  
 <211> 211  
 <212> PRT  
 <213> E. Coli

<400> 296  
 Met Asn Lys Ala Lys Arg Leu Glu Ile Leu Thr Arg Leu Arg Glu Asn  
 1 5 10 15  
 Asn Pro His Pro Thr Thr Glu Leu Asn Phe Ser Ser Pro Phe Glu Leu  
 20 25 30  
 Leu Ile Ala Val Leu Leu Ser Ala Gln Ala Thr Asp Val Ser Val Asn  
 35 40 45  
 Lys Ala Thr Ala Lys Leu Tyr Pro Val Ala Asn Thr Pro Ala Ala Met  
 50 55 60  
 Leu Glu Leu Gly Val Glu Gly Val Lys Thr Tyr Ile Lys Thr Ile Gly  
 65 70 75 80  
 Leu Tyr Asn Ser Lys Ala Glu Asn Ile Ile Lys Thr Cys Arg Ile Leu  
 85 90 95  
 Leu Glu Gln His Asn Gly Glu Val Pro Glu Asp Arg Ala Ala Leu Glu  
 100 105 110  
 Ala Leu Pro Gly Val Gly Arg Lys Thr Ala Asn Val Val Leu Asn Thr  
 115 120 125  
 Ala Phe Gly Trp Pro Thr Ile Ala Val Asp Thr His Ile Phe Arg Val  
 130 135 140  
 Cys Asn Arg Thr Gln Phe Ala Pro Gly Lys Asn Val Glu Gln Val Glu  
 145 150 155 160  
 Glu Lys Leu Leu Lys Val Val Pro Ala Glu Phe Lys Val Asp Cys His  
 165 170 175  
 His Trp Leu Ile Leu His Gly Arg Tyr Thr Cys Ile Ala Arg Lys Pro  
 180 185 190  
 Arg Cys Gly Ser Cys Ile Ile Glu Asp Leu Cys Glu Tyr Lys Glu Lys  
 195 200 205  
 Val Asp Ile  
 210

<210> 297  
 <211> 167  
 <212> PRT  
 <213> E. Coli

<400> 297  
 Met Lys Arg Leu His Lys Arg Phe Leu Leu Ala Thr Phe Cys Ala Leu  
 1 5 10 15  
 Phe Thr Ala Thr Leu Gln Ala Ala Asp Val Thr Ile Thr Val Asn Gly  
 20 25 30  
 Arg Val Val Ala Lys Pro Cys Thr Ile Gln Thr Lys Glu Ala Asn Val  
 35 40 45  
 Asn Leu Gly Asp Leu Tyr Thr Arg Asn Leu Gln Gln Pro Gly Ser Ala  
 50 55 60  
 Ser Gly Trp His Asn Ile Thr Leu Ser Leu Thr Asp Cys Pro Val Glu

65					70					75				80
Thr	Ser	Ala	Val	Thr	Ala	Ile	Val	Thr	Gly	Ser	Thr	Asp	Asn	Thr
				85					90				95	Gly
Tyr	Tyr	Lys	Asn	Glu	Gly	Thr	Ala	Glu	Asn	Ile	Gln	Ile	Glu	Leu
			100					105					110	Arg
Asp	Asp	Gln	Asp	Ala	Ala	Leu	Lys	Asn	Gly	Asp	Ser	Lys	Thr	Val
		115					120					125		Ile
Val	Asp	Glu	Ile	Thr	Arg	Asn	Ala	Gln	Phe	Pro	Leu	Lys	Ala	Arg
	130					135					140			Ala
Ile	Thr	Val	Asn	Gly	Asn	Ala	Ser	Gln	Gly	Thr	Ile	Glu	Ala	Leu
145					150				155					160
Asn	Val	Ile	Tyr	Thr	Trp	Gln								
				165										

<210> 298  
 <211> 176  
 <212> PRT  
 <213> E. Coli

Met	Lys	Tyr	Asn	Asn	Ile	Ile	Phe	Leu	Gly	Leu	Cys	Leu	Gly	Leu
1				5					10				15	Thr
Thr	Tyr	Ser	Ala	Leu	Ser	Ala	Asp	Ser	Val	Ile	Lys	Ile	Ser	Gly
			20				25					30		Arg
Val	Leu	Asp	Tyr	Gly	Cys	Thr	Val	Ser	Ser	Asp	Ser	Leu	Asn	Phe
	35					40					45			Thr
Val	Asp	Leu	Gln	Lys	Asn	Ser	Ala	Arg	Gln	Phe	Pro	Thr	Thr	Gly
	50				55				60					Ser
Thr	Ser	Pro	Ala	Val	Pro	Phe	Gln	Ile	Thr	Leu	Ser	Glu	Cys	Ser
65				70				75						Lys
Gly	Thr	Thr	Gly	Val	Arg	Val	Ala	Phe	Asn	Gly	Ile	Glu	Asp	Ala
			85					90					95	Glu
Asn	Asn	Thr	Leu	Leu	Lys	Leu	Asp	Glu	Gly	Ser	Asn	Thr	Ala	Ser
		100					105					110		Gly
Leu	Gly	Ile	Glu	Ile	Leu	Asp	Ala	Asn	Met	Arg	Pro	Val	Lys	Leu
	115					120					125			Asn
Asp	Leu	His	Ala	Gly	Met	Gln	Trp	Ile	Pro	Leu	Val	Pro	Glu	Gln
	130				135				140					Asn
Asn	Ile	Leu	Pro	Tyr	Ser	Ala	Arg	Leu	Lys	Ser	Thr	Gln	Lys	Ser
145				150					155					Val
Asn	Pro	Gly	Leu	Val	Arg	Ala	Ser	Ala	Thr	Phe	Thr	Leu	Glu	Phe
			165					170					175	Gln

<210> 299  
 <211> 382  
 <212> PRT  
 <213> E. Coli

Met	Ser	Gly	Tyr	Thr	Val	Lys	Pro	Pro	Thr	Gly	Asp	Thr	Asn	Glu
1				5					10				15	Gln
Thr	Gln	Phe	Ile	Asp	Tyr	Phe	Asn	Leu	Phe	Tyr	Ser	Lys	Arg	Gly
			20				25					30		Gln
Glu	Gln	Ile	Ser	Ile	Ser	Gln	Gln	Leu	Gly	Asn	Tyr	Gly	Thr	Thr
	35					40					45			Phe
Phe	Ser	Ala	Ser	Arg	Gln	Ser	Tyr	Trp	Asn	Thr	Ser	Arg	Ser	Asp
	50					55					60			Gln

Gln Ile Ser Phe Gly Leu Asn Val Pro Phe Gly Asp Ile Thr Thr Ser  
 65 70 75 80  
 Leu Asn Tyr Ser Tyr Ser Asn Asn Ile Trp Gln Asn Asp Arg Asp His  
 85 90 95  
 Leu Leu Ala Phe Thr Leu Asn Val Pro Phe Ser His Trp Met Arg Thr  
 100 105 110  
 Asp Ser Gln Ser Ala Phe Arg Asn Ser Asn Ala Ser Tyr Ser Met Ser  
 115 120 125  
 Asn Asp Leu Lys Gly Gly Met Thr Asn Leu Ser Gly Val Tyr Gly Thr  
 130 135 140  
 Leu Leu Pro Asp Asn Asn Leu Asn Tyr Ser Val Gln Val Gly Asn Thr  
 145 150 155 160  
 His Gly Gly Asn Thr Ser Ser Gly Thr Ser Gly Tyr Ser Ser Leu Asn  
 165 170 175  
 Tyr Arg Gly Ala Tyr Gly Asn Thr Asn Val Gly Tyr Ser Arg Ser Gly  
 180 185 190  
 Asp Ser Ser Gln Ile Tyr Tyr Gly Met Ser Gly Gly Ile Ile Ala His  
 195 200 205  
 Ala Asp Gly Ile Thr Phe Gly Gln Pro Leu Gly Asp Thr Met Val Leu  
 210 215 220  
 Val Lys Ala Pro Gly Ala Asp Asn Val Lys Ile Glu Asn Gln Thr Gly  
 225 230 235 240  
 Ile His Thr Asp Trp Arg Gly Tyr Ala Ile Leu Pro Phe Ala Thr Glu  
 245 250 255  
 Tyr Arg Glu Asn Arg Val Ala Leu Asn Ala Asn Ser Leu Ala Asp Asn  
 260 265 270  
 Val Glu Leu Asp Glu Thr Val Val Thr Val Ile Pro Thr His Gly Ala  
 275 280 285  
 Ile Ala Arg Ala Thr Phe Asn Ala Gln Ile Gly Gly Lys Val Leu Met  
 290 295 300  
 Thr Leu Lys Tyr Gly Asn Lys Ser Val Pro Phe Gly Ala Ile Val Thr  
 305 310 315 320  
 His Gly Glu Asn Lys Asn Gly Ser Ile Val Ala Glu Asn Gly Gln Val  
 325 330 335  
 Tyr Leu Thr Gly Leu Pro Gln Ser Gly Gln Leu Gln Val Ser Trp Gly  
 340 345 350  
 Lys Asp Lys Asn Ser Asn Cys Ile Val Glu Tyr Lys Leu Pro Glu Val  
 355 360 365  
 Ser Pro Gly Thr Leu Leu Asn Gln Gln Thr Ala Ile Cys Arg  
 370 375 380

&lt;210&gt; 300

&lt;211&gt; 138

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 300

Met Ile Ala Ile Ala Asp Ile Leu Gln Ala Gly Glu Lys Leu Thr Ala  
 1 5 10 15  
 Val Ala Pro Phe Leu Ala Gly Ile Gln Asn Glu Glu Gln Tyr Thr Gln  
 20 25 30  
 Ala Leu Glu Leu Val Asp His Leu Leu Asn Asp Pro Glu Asn Pro  
 35 40 45  
 Leu Leu Asp Leu Val Cys Ala Lys Ile Thr Ala Trp Glu Glu Ser Ala  
 50 55 60  
 Pro Glu Phe Ala Glu Phe Asn Ala Met Ala Gln Ala Met Pro Gly Gly  
 65 70 75 80  
 Ile Ala Val Ile Arg Thr Leu Met Asp Gln Tyr Gly Leu Thr Leu Ser  
 85 90 95  
 Asp Leu Pro Glu Ile Gly Ser Lys Ser Met Val Ser Arg Val Leu Ser

100 105 110  
 Gly Lys Arg Lys Leu Thr Leu Glu His Ala Lys Lys Leu Ala Thr Arg  
 115 120 125  
 Phe Gly Ile Ser Pro Ala Leu Phe Ile Asp  
 130 135

<210> 301  
 <211> 104  
 <212> PRT  
 <213> E. Coli

<400> 301  
 Met His Leu Ile Thr Gln Lys Ala Leu Lys Asp Ala Ala Glu Lys Tyr  
 1 5 10 15  
 Pro Gln His Lys Thr Glu Leu Val Ala Leu Gly Asn Thr Ile Ala Lys  
 20 25 30  
 Gly Tyr Phe Lys Lys Pro Glu Ser Leu Lys Ala Val Phe Pro Ser Leu  
 35 40 45  
 Asp Asn Phe Lys Tyr Leu Asp Lys His Tyr Val Phe Asn Val Gly Gly  
 50 55 60  
 Asn Glu Leu Arg Val Val Ala Met Val Phe Phe Glu Ser Gln Lys Cys  
 65 70 75 80  
 Tyr Ile Arg Glu Val Met Thr His Lys Glu Tyr Asp Phe Phe Thr Ala  
 85 90 95  
 Val His Arg Thr Lys Gly Lys Lys  
 100

<210> 302  
 <211> 2383  
 <212> PRT  
 <213> E. Coli

<400> 302  
 Met Leu Ser Val Phe Thr Phe Phe Arg Cys Ala Arg Lys Gly Ala Phe  
 1 5 10 15  
 Met Leu Ala Arg Ser Gly Lys Val Ser Met Ala Thr Lys Lys Arg Ser  
 20 25 30  
 Gly Glu Glu Ile Asn Asp Arg Gln Ile Leu Cys Gly Met Gly Ile Lys  
 35 40 45  
 Leu Arg Arg Leu Thr Ala Gly Ile Cys Leu Ile Thr Gln Leu Ala Phe  
 50 55 60  
 Pro Met Ala Ala Ala Ala Gln Gly Val Val Asn Ala Ala Thr Gln Gln  
 65 70 75 80  
 Pro Val Pro Ala Gln Ile Ala Ile Ala Asn Ala Asn Thr Val Pro Tyr  
 85 90 95  
 Thr Leu Gly Ala Leu Glu Ser Ala Gln Ser Val Ala Glu Arg Phe Gly  
 100 105 110  
 Ile Ser Val Ala Glu Leu Arg Lys Leu Asn Gln Phe Arg Thr Phe Ala  
 115 120 125  
 Arg Ser Phe Asp Asn Val Arg Gln Gly Asp Glu Leu Asp Val Pro Ala  
 130 135 140  
 Gln Val Ser Glu Lys Lys Leu Thr Pro Pro Pro Gly Asn Ser Ser Asp  
 145 150 155 160  
 Asn Leu Glu Gln Gln Ile Ala Ser Thr Ser Gln Gln Ile Gly Ser Leu  
 165 170 175  
 Leu Ala Glu Asp Met Asn Ser Glu Gln Ala Ala Asn Met Ala Arg Gly  
 180 185 190  
 Trp Ala Ser Ser Gln Ala Ser Gly Ala Met Thr Asp Trp Leu Ser Arg

195	200	205
Phe Gly Thr Ala Arg Ile Thr	Leu Gly Val Asp Glu	Asp Phe Ser Leu
210	215	220
Lys Asn Ser Gln Phe Asp Phe	Leu His Pro Trp Tyr	Glu Thr Pro Asp
225	230	235
Asn Leu Phe Phe Ser Gln His	Thr Leu His Arg Thr	Asp Glu Arg Thr
245	250	255
Gln Ile Asn Asn Gly Leu Gly	Trp Arg His Phe Thr	Pro Thr Trp Met
260	265	270
Ser Gly Ile Asn Phe Phe Phe	Asp His Asp Leu Ser	Arg Tyr His Ser
275	280	285
Arg Ala Gly Ile Gly Ala Glu	Tyr Trp Arg Asp Tyr	Leu Lys Leu Ser
290	295	300
Ser Asn Gly Tyr Leu Arg Leu	Thr Asn Trp Arg Ser	Ala Pro Glu Leu
305	310	315
Asp Asn Asp Tyr Glu Ala Arg	Pro Ala Asn Gly Trp	Asp Val Arg Ala
325	330	335
Glu Ser Trp Leu Pro Ala Trp	Pro His Leu Gly Gly	Lys Leu Val Tyr
340	345	350
Glu Gln Tyr Tyr Gly Asp Glu	Val Ala Leu Phe Asp	Lys Asp Asp Arg
355	360	365
Gln Ser Asn Pro His Ala Ile	Thr Ala Gly Leu Asn	Tyr Thr Pro Phe
370	375	380
Pro Leu Met Thr Phe Ser Ala	Glu Gln Arg Gln Gly	Lys Gln Gly Glu
385	390	395
Asn Asp Thr Arg Phe Ala Val	Asp Phe Thr Trp Gln	Pro Gly Ser Ala
405	410	415
Met Gln Lys Gln Leu Asp Pro	Asn Glu Val Ala Ala	Arg Arg Ser Leu
420	425	430
Ala Gly Ser Arg Tyr Asp Leu	Val Asp Arg Asn Asn	Asn Ile Val Leu
435	440	445
Glu Tyr Arg Lys Lys Glu Leu	Val Arg Leu Thr Leu	Thr Asp Pro Val
450	455	460
Thr Gly Lys Ser Gly Glu Val	Lys Ser Leu Val Ser	Ser Leu Gln Thr
465	470	475
Lys Tyr Ala Leu Lys Gly Tyr	Asn Val Glu Ala Thr	Ala Leu Glu Ala
485	490	495
Ala Gly Gly Lys Val Val Thr	Thr Gly Lys Asp Ile	Leu Val Thr Leu
500	505	510
Pro Ala Tyr Arg Phe Thr Ser	Thr Pro Glu Thr Asp	Asn Thr Trp Pro
515	520	525
Ile Glu Val Thr Ala Glu Asp	Val Lys Gly Asn Leu	Ser Asn Arg Glu
530	535	540
Gln Ser Met Val Val Val Gln	Ala Pro Thr Leu Ser	Gln Lys Asp Ser
545	550	555
Ser Val Ser Leu Ser Thr Gln	Thr Leu Asn Ala Asp	Ser His Ser Thr
565	570	575
Ala Thr Leu Thr Phe Ile Ala	His Asp Ala Ala Gly	Asn Pro Val Val
580	585	590
Gly Leu Val Leu Ser Thr Arg	His Glu Gly Val Gln	Asp Ile Thr Leu
595	600	605
Ser Asp Trp Lys Asp Asn Gly	Asp Gly Ser Tyr Thr	Gln Ile Leu Thr
610	615	620
Thr Gly Ala Met Ser Gly Thr	Leu Thr Leu Met Pro	Gln Leu Asn Gly
625	630	635
Val Asp Ala Ala Lys Ala Pro	Ala Val Val Asn Ile	Ile Ser Val Ser
645	650	655
Ser Ser Arg Thr His Ser Ser	Ile Lys Ile Asp Lys	Asp Arg Tyr Leu
660	665	670
Ser Gly Asn Pro Ile Glu Val	Thr Val Glu Leu Arg	Asp Glu Asn Asp
675	680	685

Lys	Pro	Val	Lys	Glu	Gln	Lys	Gln	Gln	Leu	Asn	Asn	Ala	Val	Ser	Ile
690						695				700					
Asp	Asn	Val	Lys	Pro	Gly	Val	Thr	Thr	Asp	Trp	Lys	Glu	Thr	Ala	Asp
705					710					715					720
Gly	Val	Tyr	Lys	Ala	Thr	Tyr	Thr	Ala	Tyr	Thr	Lys	Gly	Ser	Gly	Leu
				725					730					735	
Thr	Ala	Lys	Leu	Leu	Met	Gln	Asn	Trp	Asn	Glu	Asp	Leu	His	Thr	Ala
			740					745					750		
Gly	Phe	Ile	Ile	Asp	Ala	Asn	Pro	Gln	Ser	Ala	Lys	Ile	Ala	Thr	Leu
755						760						765			
Ser	Ala	Ser	Asn	Asn	Gly	Val	Leu	Ala	Asn	Glu	Asn	Ala	Ala	Asn	Thr
770						775						780			
Val	Ser	Val	Asn	Val	Ala	Asp	Glu	Gly	Ser	Asn	Pro	Ile	Asn	Asp	His
785					790					795					800
Thr	Val	Thr	Phe	Ala	Val	Leu	Ser	Gly	Ser	Ala	Thr	Ser	Phe	Asn	Asn
			805						810					815	
Gln	Asn	Thr	Ala	Lys	Thr	Asp	Val	Asn	Gly	Leu	Ala	Thr	Phe	Asp	Leu
			820						825				830		
Lys	Ser	Ser	Lys	Gln	Glu	Asp	Asn	Thr	Val	Glu	Val	Thr	Leu	Glu	Asn
835						840						845			
Gly	Val	Lys	Gln	Thr	Leu	Ile	Val	Ser	Phe	Val	Gly	Asp	Ser	Ser	Thr
850					855						860				
Ala	Gln	Val	Asp	Leu	Gln	Lys	Ser	Lys	Asn	Glu	Val	Val	Ala	Asp	Gly
865				870						875					880
Asn	Asp	Ser	Val	Thr	Met	Thr	Ala	Thr	Val	Arg	Asp	Ala	Lys	Gly	Asn
			885						890					895	
Leu	Leu	Asn	Asp	Val	Met	Val	Thr	Phe	Asn	Val	Asn	Ser	Ala	Glu	Ala
			900					905					910		
Lys	Leu	Ser	Gln	Thr	Glu	Val	Asn	Ser	His	Asp	Gly	Ile	Ala	Thr	Ala
915						920						925			
Thr	Leu	Thr	Ser	Leu	Lys	Asn	Gly	Asp	Tyr	Arg	Val	Thr	Ala	Ser	Val
930					935						940				
Ser	Ser	Gly	Ser	Gln	Ala	Asn	Gln	Gln	Val	Asn	Phe	Ile	Gly	Asp	Gln
945				950						955					960
Ser	Thr	Ala	Ala	Leu	Thr	Leu	Ser	Val	Pro	Ser	Gly	Asp	Ile	Thr	Val
			965						970					975	
Thr	Asn	Thr	Ala	Pro	Gln	Tyr	Met	Thr	Ala	Thr	Leu	Gln	Asp	Lys	Asn
			980					985					990		
Gly	Asn	Pro	Leu	Lys	Asp	Lys	Glu	Ile	Thr	Phe	Ser	Val	Pro	Asn	Asp
		995					1000					1005			
Val	Ala	Ser	Lys	Phe	Ser	Ile	Ser	Asn	Gly	Gly	Lys	Gly	Met	Thr	Asp
	1010					1015					1020				
Ser	Asn	Gly	Val	Ala	Ile	Ala	Ser	Leu	Thr	Gly	Thr	Leu	Ala	Gly	Thr
1025				1030						1035					1040
His	Met	Ile	Met	Ala	Arg	Leu	Ala	Asn	Ser	Asn	Val	Ser	Asp	Ala	Gln
			1045					1050						1055	
Pro	Met	Thr	Phe	Val	Ala	Asp	Lys	Asp	Arg	Ala	Val	Val	Val	Leu	Gln
			1060					1065					1070		
Thr	Ser	Lys	Ala	Glu	Ile	Ile	Gly	Asn	Gly	Val	Asp	Glu	Thr	Thr	Leu
		1075					1080					1085			
Thr	Ala	Thr	Val	Lys	Asp	Pro	Ser	Asn	His	Pro	Val	Ala	Gly	Ile	Thr
	1090					1095					1100				
Val	Asn	Phe	Thr	Met	Pro	Gln	Asp	Val	Ala	Ala	Asn	Phe	Thr	Leu	Glu
1105				1110						1115					1120
Asn	Asn	Gly	Ile	Ala	Ile	Thr	Gln	Ala	Asn	Gly	Glu	Ala	His	Val	Thr
			1125					1130						1135	
Leu	Lys	Gly	Lys	Ala	Gly	Thr	His	Thr	Val	Thr	Ala	Thr	Leu	Gly	
		1140					1145					1150			
Asn	Asn	Asn	Thr	Ser	Asp	Ser	Gln	Pro	Val	Thr	Phe	Val	Ala	Asp	Lys
		1155					1160					1165			
Ala	Ser	Ala	Gln	Val	Val	Leu	Gln	Ile	Ser	Lys	Asp	Glu	Ile	Thr	Gly



1170	1175	1180
Asn Gly Val Asp Ser	Ala Thr Leu Thr	Ala Thr Val Lys Asp Gln Phe
1185	1190	1195
Asp Asn Glu Val Asn Asn	Leu Pro Val Thr Phe Ser Ser	Ala Ser Ser
1205	1210	1215
Gly Leu Thr Leu Thr Pro	Gly Val Ser Asn Thr Asn	Glu Ser Gly Ile
1220	1225	1230
Ala Gln Ala Thr Leu Ala	Gly Val Ala Phe Gly Glu	Lys Thr Val Thr
1235	1240	1245
Ala Ser Leu Ala Asn Asn	Gly Ala Ser Asp Asn	Lys Thr Val His Phe
1250	1255	1260
Ile Gly Asp Thr Ala Ala	Ala Lys Ile Ile Glu	Leu Ala Pro Val Pro
1265	1270	1275
Asp Ser Ile Ile Ala Gly	Thr Pro Gln Asn Ser Ser	Gly Ser Val Ile
1285	1290	1295
Thr Ala Thr Val Val Asp	Asn Asn Gly Phe Pro	Val Lys Gly Val Thr
1300	1305	1310
Val Asn Phe Thr Ser Asn	Ala Ala Thr Ala Glu	Met Thr Asn Gly Gly
1315	1320	1325
Gln Ala Val Thr Asn Glu	Gln Gly Lys Ala Thr	Val Thr Tyr Thr Asn
1330	1335	1340
Thr Arg Ser Ser Ile Glu	Ser Gly Ala Arg Pro	Asp Thr Val Glu Ala
1345	1350	1355
Ser Leu Glu Asn Gly Ser	Ser Thr Leu Ser Thr	Ser Ile Asn Val Asn
1365	1370	1375
Ala Asp Ala Ser Thr Ala	His Leu Thr Leu Leu	Gln Ala Leu Phe Asp
1380	1385	1390
Thr Val Ser Ala Gly Glu	Thr Thr Ser Leu Tyr	Ile Glu Val Lys Asp
1395	1400	1405
Asn Tyr Gly Asn Gly Val	Pro Gln Gln Glu Val	Thr Leu Ser Val Ser
1410	1415	1420
Pro Ser Glu Gly Val Thr	Pro Ser Asn Asn Ala	Ile Tyr Thr Thr Asn
1425	1430	1435
His Asp Gly Asn Phe Tyr	Ala Ser Phe Thr Ala	Thr Lys Ala Gly Val
1445	1450	1455
Tyr Gln Leu Thr Ala Thr	Leu Glu Asn Gly Asp	Ser Met Gln Gln Thr
1460	1465	1470
Val Thr Tyr Val Pro Asn	Val Ala Asn Ala Glu	Ile Thr Leu Ala Ala
1475	1480	1485
Ser Lys Asp Pro Val Ile	Ala Asp Asn Asn Asp	Leu Thr Thr Leu Thr
1490	1495	1500
Ala Thr Val Ala Asp Thr	Glu Gly Asn Ala Ile	Ala Asn Thr Glu Val
1505	1510	1515
Thr Phe Thr Leu Pro Glu	Asp Val Lys Ala Asn	Phe Thr Leu Ser Asp
1525	1530	1535
Gly Gly Lys Val Ile Thr	Asp Ala Glu Gly Lys	Ala Lys Val Thr Leu
1540	1545	1550
Lys Gly Thr Lys Ala Gly	Ala His Thr Val Thr	Ala Ser Met Thr Gly
1555	1560	1565
Gly Lys Ser Glu Gln Leu	Val Val Asn Phe Ile	Ala Asp Thr Leu Thr
1570	1575	1580
Ala Gln Val Asn Leu Asn	Val Thr Glu Asp Asn	Phe Ile Ala Asn Asn
1585	1590	1595
Val Gly Met Thr Arg Leu	Gln Ala Thr Val Thr	Asp Gly Asn Gly Asn
1605	1610	1615
Pro Leu Ala Asn Glu Ala	Val Thr Phe Thr Leu	Pro Ala Asp Val Ser
1620	1625	1630
Ala Ser Phe Thr Leu Gly	Gln Gly Ser Ala Ile	Thr Asp Ile Asn
1635	1640	1645
Gly Lys Ala Glu Val Thr	Leu Ser Gly Thr Lys	Ser Gly Thr Tyr Pro
1650	1655	1660

Val Thr Val Ser Val	Asn Asn Tyr Gly Val	Ser Asp Thr Lys Gln Val	1665	1670	1675	1680
Thr Leu Ile Ala Asp	Ala Gly Thr Ala Lys	Leu Ala Ser Leu Thr Ser	1685	1690	1695	
Val Tyr Ser Phe Val	Val Ser Thr Thr Glu	Gly Ala Thr Met Thr Ala	1700	1705	1710	
Ser Val Thr Asp Ala	Asn Gly Asn Pro Val	Glu Gly Ile Lys Val Asn	1715	1720	1725	
Phe Arg Gly Thr Ser	Val Thr Leu Ser Ser	Thr Ser Val Glu Thr Asp	1730	1735	1740	
Asp Arg Gly Phe Ala	Glu Ile Leu Val Thr	Ser Thr Glu Val Gly Leu	1745	1750	1755	1760
Lys Thr Val Ser Ala	Ser Leu Ala Asp Lys	Pro Thr Glu Val Ile Ser	1765	1770	1775	
Arg Leu Leu Asn Ala	Ser Ala Asp Val Asn	Ser Ala Thr Ile Thr Ser	1780	1785	1790	
Leu Glu Ile Pro Glu	Gly Gln Val Met Val	Ala Gln Asp Val Ala Val	1795	1800	1805	
Lys Ala His Val Asn	Asp Gln Phe Gly Asn	Pro Val Ala His Gln Pro	1810	1815	1820	
Val Thr Phe Ser Ala	Glu Pro Ser Ser Gln	Met Ile Ile Ser Gln Asn	1825	1830	1835	1840
Thr Val Ser Thr Asn	Thr Gln Gly Val Ala	Glu Val Thr Met Thr Pro	1845	1850	1855	
Glu Arg Asn Gly Ser	Tyr Met Val Lys Ala	Ser Leu Pro Asn Gly Ala	1860	1865	1870	
Ser Leu Glu Lys Gln	Leu Glu Ala Ile Asp	Glu Lys Leu Thr Leu Thr	1875	1880	1885	
Ala Ser Ser Pro Leu	Ile Gly Val Tyr Ala	Pro Thr Gly Ala Thr Leu	1890	1895	1900	
Thr Ala Thr Leu Thr	Ser Ala Asn Gly Thr	Pro Val Glu Gly Gln Val	1905	1910	1915	1920
Ile Asn Phe Ser Val	Thr Pro Glu Gly Ala	Thr Leu Ser Gly Gly Lys	1925	1930	1935	
Val Arg Thr Asn Ser	Ser Gly Gln Ala Pro	Val Val Leu Thr Ser Asn	1940	1945	1950	
Lys Val Gly Thr Tyr	Thr Val Thr Ala Ser	Phe His Asn Gly Val Thr	1955	1960	1965	
Ile Gln Thr Gln Thr	Thr Val Lys Val Thr	Gly Asn Ser Ser Thr Ala	1970	1975	1980	
His Val Ala Ser Phe	Ile Ala Asp Pro Ser	Thr Ile Ala Ala Thr Asn	1985	1990	1995	2000
Thr Asp Leu Ser Thr	Leu Lys Ala Thr Val	Glu Asp Gly Ser Gly Asn	2005	2010	2015	
Leu Ile Glu Gly Leu	Thr Val Tyr Phe Ala	Leu Lys Ser Gly Ser Ala	2020	2025	2030	
Thr Leu Thr Ser Leu	Thr Ala Val Thr Asp	Gln Asn Gly Ile Ala Thr	2035	2040	2045	
Thr Ser Val Lys Gly	Ala Met Thr Gly Ser	Val Thr Val Ser Ala Val	2050	2055	2060	
Thr Thr Ala Gly Gly	Met Gln Thr Val Asp	Ile Thr Leu Val Ala Gly	2065	2070	2075	2080
Pro Ala Asp Thr Ser	Gln Ser Val Leu Lys	Ser Asn Arg Ser Ser Leu	2085	2090	2095	
Lys Gly Asp Tyr Thr	Asp Ser Ala Glu Leu	Arg Leu Val Leu His Asp	2100	2105	2110	
Ile Ser Gly Asn Pro	Ile Lys Val Ser Glu	Gly Met Glu Phe Val Gln	2115	2120	2125	
Ser Gly Thr Asn Val	Pro Tyr Ile Lys Ile	Ser Ala Ile Asp Tyr Ser	2130	2135	2140	
Leu Asn Ile Asn Gly	Asp Tyr Lys Ala Thr	Val Thr Gly Gly Gly Glu				

2145                      2150                      2155                      2160  
 Gly Ile Ala Thr Leu Ile Pro Val Leu Asn Gly Val His Gln Ala Gly  
                                  2165                      2170                      2175  
 Leu Ser Thr Thr Ile Gln Phe Thr Arg Ala Glu Asp Lys Ile Met Ser  
                                  2180                      2185                      2190  
 Gly Thr Val Ser Val Asn Gly Thr Asp Leu Pro Thr Thr Thr Phe Pro  
                                  2195                      2200                      2205  
 Ser Gln Gly Phe Thr Gly Ala Tyr Tyr Gln Leu Asn Asn Asp Asn Phe  
                                  2210                      2215                      2220  
 Ala Pro Gly Lys Thr Ala Ala Asp Tyr Glu Phe Ser Ser Ser Ala Ser  
 2225                      2230                      2235                      2240  
 Trp Val Asp Val Asp Ala Thr Gly Lys Val Thr Phe Lys Asn Val Gly  
                                  2245                      2250                      2255  
 Ser Asn Ser Glu Arg Ile Thr Ala Thr Pro Lys Ser Gly Gly Pro Ser  
                                  2260                      2265                      2270  
 Tyr Val Tyr Glu Ile Arg Val Lys Ser Trp Trp Val Asn Ala Gly Glu  
                                  2275                      2280                      2285  
 Ala Phe Met Ile Tyr Ser Leu Ala Glu Asn Phe Cys Ser Ser Asn Gly  
                                  2290                      2295                      2300  
 Tyr Thr Leu Pro Arg Ala Asn Tyr Leu Asn His Cys Ser Ser Arg Gly  
 2305                      2310                      2315                      2320  
 Ile Gly Ser Leu Tyr Ser Glu Trp Gly Asp Met Gly His Tyr Thr Thr  
                                  2325                      2330                      2335  
 Asp Ala Gly Phe Gln Ser Asn Met Tyr Trp Ser Ser Ser Pro Ala Asn  
                                  2340                      2345                      2350  
 Ser Ser Glu Gln Tyr Val Val Ser Leu Ala Thr Gly Asp Gln Ser Val  
                                  2355                      2360                      2365  
 Phe Glu Lys Leu Gly Phe Ala Tyr Ala Thr Cys Tyr Lys Asn Leu  
                                  2370                      2375                      2380

<210> 303  
 <211> 61  
 <212> PRT  
 <213> E. Coli

<400> 303  
 Met Ser Lys Gly Ala Leu Tyr Glu Phe Asn Asn Pro Asp Gln Leu Lys  
 1                      5                      10                      15  
 Ile Pro Leu Pro His Lys His Ile Ala Ser Thr Phe Asn Asp Ile Met  
                                  20                      25                      30  
 Ser Lys Asp Val Gly Tyr Ala Tyr Val Ser Leu Leu Tyr Ala Cys Pro  
                                  35                      40                      45  
 Leu Lys Thr His Ser Leu Arg Leu Asn Pro Phe Ser Lys  
                                  50                      55                      60

<210> 304  
 <211> 398  
 <212> PRT  
 <213> E. Coli

<400> 304  
 Met Gln Val Ala Glu Gln Arg Ile Gln Leu Ala Glu Ala Gln Ala Lys  
 1                      5                      10                      15  
 Ala Val Ala Thr Gln Asp Gly Pro Gln Ile Asp Phe Ser Ala Asp Met  
                                  20                      25                      30  
 Glu Arg Gln Lys Met Ser Ala Glu Gly Leu Met Gly Pro Phe Ala Leu  
                                  35                      40                      45  
 Asn Asp Pro Ala Ala Gly Thr Thr Gly Pro Trp Tyr Thr Asn Gly Thr  
                                  50                      55                      60

Phe Gly Leu Thr Ala Gly Trp His Leu Asp Ile Trp Gly Lys Asn Arg  
 65 70 75 80  
 Ala Glu Val Thr Ala Arg Leu Gly Thr Val Lys Ala Arg Ala Ala Glu  
 85 90 95  
 Arg Glu Gln Thr Arg Gln Leu Leu Ala Gly Ser Val Ala Arg Leu Tyr  
 100 105 110  
 Trp Glu Trp Gln Thr Gln Ala Ala Leu Asn Thr Val Leu Gln Gln Ile  
 115 120 125  
 Glu Lys Glu Gln Asn Thr Ile Ile Ala Thr Asp Arg Gln Leu Tyr Gln  
 130 135 140  
 Asn Gly Ile Thr Ser Ser Val Glu Gly Val Glu Thr Asp Ile Asn Ala  
 145 150 155 160  
 Ser Lys Thr Arg Gln Gln Leu Asn Asp Val Ala Gly Lys Met Lys Ile  
 165 170 175  
 Ile Glu Ala Arg Leu Ser Ala Leu Thr Asn Asn Gln Thr Lys Ser Leu  
 180 185 190  
 Lys Leu Lys Pro Val Ala Leu Pro Lys Val Ala Ser Gln Leu Pro Asp  
 195 200 205  
 Glu Leu Gly Tyr Ser Leu Leu Ala Arg Arg Ala Asp Leu Gln Ala Ala  
 210 215 220  
 His Trp Tyr Val Glu Ser Ser Leu Ser Thr Ile Asp Ala Ala Lys Ala  
 225 230 235 240  
 Ala Phe Tyr Pro Asp Ile Asn Leu Met Ala Phe Leu Gln Gln Asp Ala  
 245 250 255  
 Leu His Leu Ser Asp Leu Phe Arg His Ser Ala Gln Gln Met Gly Val  
 260 265 270  
 Thr Ala Gly Leu Thr Leu Pro Ile Phe Asp Ser Gly Arg Leu Asn Ala  
 275 280 285  
 Asn Leu Asp Ile Ala Lys Ala Glu Ser Asn Leu Ser Ile Ala Ser Tyr  
 290 295 300  
 Asn Lys Ala Val Val Glu Ala Val Asn Asp Val Ala Arg Ala Ala Ser  
 305 310 315 320  
 Gln Val Gln Thr Leu Ala Glu Lys Asn Gln His Gln Ala Gln Ile Glu  
 325 330 335  
 Arg Asp Ala Leu Arg Val Val Gly Leu Ala Gln Ala Arg Phe Asn Ala  
 340 345 350  
 Gly Ile Ile Ala Gly Ser Arg Val Ser Glu Ala Arg Ile Pro Ala Leu  
 355 360 365  
 Arg Glu Arg Ala Asn Gly Leu Leu Leu Gln Gly Gln Trp Leu Asp Ala  
 370 375 380  
 Ser Ile Gln Leu Thr Gly Ala Leu Gly Gly Gly Tyr Lys Arg  
 385 390 395

&lt;210&gt; 305

&lt;211&gt; 96

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 305

Met Tyr Cys His Ala Lys Leu Lys Asn Ile Ser Gln His Thr Val Ile  
 1 5 10 15  
 Ser Ala His Leu Phe Leu Pro Asp Tyr Ser Pro Met Asn Arg Asp Ser  
 20 25 30  
 Phe Tyr Pro Ala Ile Ala Cys Phe Pro Leu Leu Leu Met Leu Ala Gly  
 35 40 45  
 Cys Ala Pro Met His Glu Thr Arg Gln Ala Leu Ser Gln Gln Thr Pro  
 50 55 60  
 Ala Ala Gln Val Asp Thr Ala Leu Pro Thr Ala Leu Lys Met Val Gly  
 65 70 75 80  
 Gln Thr Ala Asn Gly Gly Trp Ser Ile Thr Ile Ile Asn Ser Leu Pro

85

90

95

<210> 306  
 <211> 315  
 <212> PRT  
 <213> E. Coli

<400> 306  
 Met Arg Val Leu Leu Ala Pro Met Glu Gly Val Leu Asp Ser Leu Val  
 1 5 10 15  
 Arg Glu Leu Leu Thr Glu Val Asn Asp Tyr Asp Leu Cys Ile Thr Glu  
 20 25 30  
 Phe Val Arg Val Val Asp Gln Leu Leu Pro Val Lys Val Phe His Arg  
 35 40 45  
 Ile Cys Pro Glu Leu Gln Asn Ala Ser Arg Thr Pro Ser Gly Thr Leu  
 50 55 60  
 Val Arg Val Gln Leu Leu Gly Gln Phe Pro Gln Trp Leu Ala Glu Asn  
 65 70 75 80  
 Ala Ala Arg Ala Val Glu Leu Gly Ser Trp Gly Val Asp Leu Asn Cys  
 85 90 95  
 Gly Cys Pro Ser Lys Thr Val Asn Gly Ser Gly Gly Gly Ala Thr Leu  
 100 105 110  
 Leu Lys Asp Pro Glu Leu Ile Tyr Gln Gly Ala Lys Ala Met Arg Glu  
 115 120 125  
 Ala Val Pro Ala His Leu Pro Val Ser Val Lys Val Arg Leu Gly Trp  
 130 135 140  
 Asp Ser Gly Glu Lys Lys Phe Glu Ile Ala Asp Ala Val Gln Gln Ala  
 145 150 155 160  
 Gly Ala Thr Glu Leu Val Val His Gly Arg Thr Lys Glu Gln Gly Tyr  
 165 170 175  
 Arg Ala Glu His Ile Asp Trp Gln Ala Ile Gly Asp Ile Arg Gln Arg  
 180 185 190  
 Leu Asn Ile Pro Val Ile Ala Asn Gly Glu Ile Trp Asp Trp Gln Ser  
 195 200 205  
 Ala Gln Gln Cys Met Ala Ile Ser Gly Cys Asp Ala Val Met Ile Gly  
 210 215 220  
 Arg Gly Ala Leu Asn Ile Pro Asn Leu Ser Arg Val Val Lys Tyr Asn  
 225 230 235 240  
 Glu Pro Arg Met Pro Trp Pro Glu Val Val Ala Leu Leu Gln Lys Tyr  
 245 250 255  
 Thr Arg Leu Glu Lys Gln Gly Asp Thr Gly Leu Tyr His Val Ala Arg  
 260 265 270  
 Ile Lys Gln Trp Leu Ser Tyr Leu Arg Lys Glu Tyr Asp Glu Ala Thr  
 275 280 285  
 Glu Leu Phe Gln His Val Arg Val Leu Asn Asn Ser Pro Asp Ile Ala  
 290 295 300  
 Arg Ala Ile Gln Ala Ile Asp Ile Glu Lys Leu  
 305 310 315

<210> 307  
 <211> 296  
 <212> PRT  
 <213> E. Coli

<400> 307  
 Met Thr Ile Ser Thr Thr Ser Thr Pro His Asp Ala Val Phe Lys Ser  
 1 5 10 15  
 Phe Leu Arg His Pro Asp Thr Ala Arg Asp Phe Ile Asp Ile His Leu  
 20 25 30

Pro Ala Pro Leu Arg Lys Leu Cys Asp Leu Thr Thr Leu Lys Leu Glu  
 35 40 45  
 Pro Asn Ser Phe Ile Asp Glu Asp Leu Arg Gln Tyr Tyr Ser Asp Leu  
 50 55 60  
 Leu Trp Ser Val Lys Thr Gln Glu Gly Val Gly Tyr Ile Tyr Val Val  
 65 70 75 80  
 Ile Glu His Gln Ser Lys Pro Glu Glu Leu Met Ala Phe Arg Met Met  
 85 90 95  
 Arg Tyr Ser Ile Ala Ala Met Gln Asn His Leu Asp Ala Gly Tyr Lys  
 100 105 110  
 Glu Leu Pro Leu Val Leu Pro Met Leu Phe Tyr His Gly Cys Arg Ser  
 115 120 125  
 Pro Tyr Pro Tyr Ser Leu Cys Trp Leu Asp Glu Phe Ala Glu Pro Ala  
 130 135 140  
 Ile Ala Arg Lys Ile Tyr Ser Ser Ala Phe Pro Leu Val Asp Ile Thr  
 145 150 155 160  
 Val Val Pro Asp Asp Glu Ile Met Gln His Arg Lys Met Ala Leu Leu  
 165 170 175  
 Glu Leu Ile Gln Lys His Ile Arg Gln Arg Asp Leu Leu Gly Leu Val  
 180 185 190  
 Asp Gln Ile Val Ser Leu Leu Val Thr Gly Asn Thr Asn Asp Arg Gln  
 195 200 205  
 Leu Lys Ala Leu Phe Asn Tyr Val Leu Gln Thr Gly Asp Ala Gln Arg  
 210 215 220  
 Phe Arg Ala Phe Ile Gly Glu Ile Ala Glu Arg Ala Pro Gln Glu Lys  
 225 230 235 240  
 Glu Lys Leu Met Thr Ile Ala Asp Arg Leu Arg Glu Glu Gly Ala Met  
 245 250 255  
 Gln Gly Lys His Glu Glu Ala Leu Arg Ile Ala Gln Glu Met Leu Asp  
 260 265 270  
 Arg Gly Leu Asp Arg Glu Leu Val Met Met Val Thr Arg Leu Ser Pro  
 275 280 285  
 Asp Asp Leu Ile Ala Gln Ser His  
 290 295

<210> 308  
 <211> 555  
 <212> PRT  
 <213> E. Coli

<400> 308

<400> 3

Met Ala Gln Phe Val Tyr Thr Met His Arg Val Gly Lys Val Val Pro  
 1 5 10 15  
 Pro Lys Arg His Ile Leu Lys Asn Ile Ser Leu Ser Phe Phe Pro Gly  
 20 25 30  
 Ala Lys Ile Gly Val Leu Gly Leu Asn Gly Ala Gly Lys Ser Thr Leu  
 35 40 45  
 Leu Arg Ile Met Ala Gly Ile Asp Lys Asp Ile Glu Gly Glu Ala Arg  
 50 55 60  
 Pro Gln Pro Asp Ile Lys Ile Gly Tyr Leu Pro Gln Glu Pro Gln Leu  
 65 70 75 80  
 Asn Pro Glu His Thr Val Arg Glu Ser Ile Glu Glu Ala Val Ser Glu  
 85 90 95  
 Val Val Asn Ala Leu Lys Arg Leu Asp Glu Val Tyr Ala Leu Tyr Ala  
 100 105 110  
 Asp Pro Asp Ala Asp Phe Asp Lys Leu Ala Ala Glu Gln Gly Arg Leu  
 115 120 125  
 Glu Glu Ile Ile Gln Ala His Asp Gly His Asn Leu Asn Val Gln Leu  
 130 135 140

Glu	Arg	Ala	Ala	Asp	Ala	Leu	Arg	Leu	Pro	Asp	Trp	Asp	Ala	Lys	Ile
145					150					155					160
Ala	Asn	Leu	Ser	Gly	Gly	Glu	Arg	Arg	Arg	Val	Ala	Leu	Cys	Arg	Leu
				165					170					175	
Leu	Leu	Glu	Lys	Pro	Asp	Met	Leu	Leu	Leu	Asp	Glu	Pro	Thr	Asn	His
			180						185					190	
Leu	Asp	Ala	Glu	Ser	Val	Ala	Trp	Leu	Glu	Arg	Phe	Leu	His	Asp	Phe
			195				200					205			
Glu	Gly	Thr	Val	Val	Ala	Ile	Thr	His	Asp	Arg	Tyr	Phe	Leu	Asp	Asn
	210					215					220				
Val	Ala	Gly	Trp	Ile	Leu	Glu	Leu	Asp	Arg	Gly	Glu	Gly	Ile	Pro	Trp
225					230					235					240
Glu	Gly	Asn	Tyr	Ser	Ser	Trp	Leu	Glu	Gln	Lys	Asp	Gln	Arg	Leu	Ala
				245					250					255	
Gln	Glu	Ala	Ser	Gln	Glu	Ala	Ala	Arg	Arg	Lys	Ser	Ile	Glu	Lys	Glu
			260					265						270	
Leu	Glu	Trp	Val	Arg	Gln	Gly	Thr	Lys	Gly	Arg	Gln	Ser	Lys	Gly	Lys
		275					280					285			
Ala	Arg	Leu	Ala	Arg	Phe	Glu	Glu	Leu	Asn	Ser	Thr	Glu	Tyr	Gln	Lys
	290					295					300				
Arg	Asn	Glu	Thr	Asn	Glu	Leu	Phe	Ile	Pro	Pro	Gly	Pro	Arg	Leu	Gly
305					310					315					320
Asp	Lys	Val	Leu	Glu	Val	Ser	Asn	Leu	Arg	Lys	Ser	Tyr	Gly	Asp	Arg
				325					330					335	
Leu	Leu	Ile	Asp	Leu	Ser	Phe	Ser	Ile	Pro	Lys	Gly	Ala	Ile	Val	
			340				345					350			
Gly	Ile	Ile	Gly	Pro	Asn	Gly	Ala	Gly	Lys	Ser	Thr	Leu	Phe	Arg	Met
		355					360					365			
Ile	Ser	Gly	Gln	Glu	Gln	Pro	Asp	Ser	Gly	Thr	Ile	Thr	Leu	Gly	Glu
	370					375					380				
Thr	Val	Lys	Leu	Ala	Ser	Val	Asp	Gln	Phe	Arg	Asp	Ser	Met	Asp	Asn
385					390					395					400
Ser	Lys	Thr	Val	Trp	Glu	Glu	Val	Ser	Gly	Gly	Leu	Asp	Ile	Met	Lys
				405					410					415	
Ile	Gly	Asn	Thr	Glu	Met	Pro	Ser	Arg	Ala	Tyr	Val	Gly	Arg	Phe	Asn
			420					425						430	
Phe	Lys	Gly	Val	Asp	Gln	Gly	Lys	Arg	Val	Gly	Glu	Leu	Ser	Gly	Gly
		435					440					445			
Glu	Arg	Gly	Arg	Leu	His	Leu	Ala	Lys	Leu	Leu	Gln	Val	Gly	Gly	Asn
	450					455					460				
Met	Leu	Leu	Leu	Asp	Glu	Pro	Thr	Asn	Asp	Leu	Asp	Ile	Glu	Thr	Leu
465					470					475					480
Arg	Ala	Leu	Glu	Asn	Ala	Leu	Leu	Glu	Phe	Pro	Gly	Cys	Ala	Met	Val
				485					490					495	
Ile	Ser	His	Asp	Arg	Trp	Phe	Leu	Asp	Arg	Ile	Ala	Thr	His	Ile	Leu
			500					505					510		
Asp	Tyr	Gln	Asp	Glu	Gly	Lys	Val	Glu	Phe	Phe	Glu	Gly	Asn	Phe	Thr
		515					520					525			
Glu	Tyr	Glu	Glu	Tyr	Lys	Lys	Arg	Thr	Leu	Gly	Ala	Asp	Ala	Leu	Glu
	530					535					540				
Pro	Lys	Arg	Ile	Lys	Tyr	Lys	Arg	Ile	Ala	Lys					
545					550										

&lt;210&gt; 309

&lt;211&gt; 173

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 309

Met Ser Lys Pro Lys Tyr Pro Phe Glu Lys Arg Leu Glu Val Val Asn  
 1 5 10 15  
 His Tyr Phe Thr Thr Asp Asp Gly Tyr Arg Ile Ile Ser Ala Arg Phe  
 20 25 30  
 Gly Val Pro Arg Thr Gln Val Arg Thr Trp Val Ala Leu Tyr Glu Lys  
 35 40 45  
 His Gly Glu Lys Gly Leu Ile Pro Lys Pro Lys Gly Val Ser Ala Asp  
 50 55 60  
 Pro Glu Leu Arg Ile Lys Val Val Lys Ala Val Ile Glu Gln His Met  
 65 70 75 80  
 Ser Leu Asn Gln Ala Ala Ala His Phe Met Leu Ala Gly Ser Gly Ser  
 85 90 95  
 Val Ala Arg Trp Leu Lys Val Tyr Glu Glu Arg Gly Glu Ala Gly Leu  
 100 105 110  
 Arg Ala Leu Lys Ile Gly Thr Lys Arg Asn Ile Ala Ile Ser Val Asp  
 115 120 125  
 Pro Glu Lys Ala Ala Ser Ala Leu Glu Leu Ser Lys Asp Arg Arg Ile  
 130 135 140  
 Glu Asp Leu Glu Arg Gln Val Arg Phe Leu Glu Thr Arg Leu Met Tyr  
 145 150 155 160  
 Leu Lys Lys Leu Lys Ala Leu Ala His Pro Thr Lys Lys  
 165 170

<210> 310  
 <211> 283  
 <212> PRT  
 <213> E. Coli

<400> 310

Met Lys Val Leu Asn Glu Leu Arg Gln Phe Tyr Pro Leu Asp Glu Leu  
 1 5 10 15  
 Leu Arg Ala Ala Glu Ile Pro Arg Ser Thr Phe Tyr Tyr His Leu Lys  
 20 25 30  
 Ala Leu Ser Lys Pro Asp Lys Tyr Ala Asp Val Lys Lys Arg Ile Ser  
 35 40 45  
 Glu Ile Tyr His Glu Asn Arg Gly Arg Tyr Gly Tyr Arg Arg Val Thr  
 50 55 60  
 Leu Ser Leu His Arg Glu Gly Lys Gln Ile Asn His Lys Ala Val Gln  
 65 70 75 80  
 Arg Leu Met Gly Thr Leu Ser Leu Lys Ala Ala Ile Lys Val Lys Arg  
 85 90 95  
 Tyr Arg Ser Tyr Arg Gly Glu Val Gly Gln Thr Ala Pro Asn Val Leu  
 100 105 110  
 Gln Arg Asp Phe Lys Ala Thr Arg Pro Asn Glu Lys Trp Val Thr Asp  
 115 120 125  
 Val Thr Glu Phe Ala Val Asn Gly Arg Lys Leu Tyr Leu Ser Pro Val  
 130 135 140  
 Ile Asp Leu Phe Asn Asn Glu Val Ile Ser Tyr Ser Leu Ser Glu Arg  
 145 150 155 160  
 Pro Val Met Asn Met Val Glu Asn Met Leu Asp Gln Ala Phe Lys Lys  
 165 170 175  
 Leu Asn Pro His Glu His Pro Val Leu His Ser Asp Gln Gly Trp Gln  
 180 185 190  
 Tyr Arg Met Arg Arg Tyr Gln Asn Ile Leu Lys Glu His Gly Ile Lys  
 195 200 205  
 Gln Ser Met Ser Arg Lys Gly Asn Cys Leu Asp Asn Ala Val Val Glu  
 210 215 220  
 Cys Phe Phe Gly Thr Leu Lys Ser Glu Cys Phe Tyr Leu Asp Glu Phe  
 225 230 235 240  
 Ser Asn Ile Ser Glu Leu Lys Asp Ala Val Thr Glu Tyr Ile Glu Tyr



Tyr Asn Ser Arg Arg Ile Ser Leu Lys Leu Lys Gly Leu Thr Pro Ile  
 245 250 255  
 260 265 270  
 Glu Tyr Arg Asn Gln Thr Tyr Met Pro Arg Val  
 275 280

<210> 311  
 <211> 38  
 <212> PRT  
 <213> E. Coli

<400> 311  
 Met Lys Val Arg Ala Ser Val Lys Lys Leu Cys Arg Asn Cys Lys Ile  
 1 5 10 15  
 Val Lys Arg Asp Gly Val Ile Arg Val Ile Cys Ser Ala Glu Pro Lys  
 20 25 30  
 His Lys Gln Arg Gln Gly  
 35

<210> 312  
 <211> 443  
 <212> PRT  
 <213> E. Coli

<400> 312  
 Met Ala Lys Gln Pro Gly Leu Asp Phe Gln Ser Ala Lys Gly Gly Leu  
 1 5 10 15  
 Gly Glu Leu Lys Arg Arg Leu Leu Phe Val Ile Gly Ala Leu Ile Val  
 20 25 30  
 Phe Arg Ile Gly Ser Phe Ile Pro Ile Pro Gly Ile Asp Ala Ala Val  
 35 40 45  
 Leu Ala Lys Leu Leu Glu Gln Arg Gly Thr Ile Ile Glu Met Phe  
 50 55 60  
 Asn Met Phe Ser Gly Gly Ala Leu Ser Arg Ala Ser Ile Phe Ala Leu  
 65 70 75 80  
 Gly Ile Met Pro Tyr Ile Ser Ala Ser Ile Ile Ile Gln Leu Leu Thr  
 85 90 95  
 Val Val His Pro Thr Leu Ala Glu Ile Lys Lys Glu Gly Glu Ser Gly  
 100 105 110  
 Arg Arg Lys Ile Ser Gln Tyr Thr Arg Tyr Gly Thr Leu Val Leu Ala  
 115 120 125  
 Ile Phe Gln Ser Ile Gly Ile Ala Thr Gly Leu Pro Asn Met Pro Gly  
 130 135 140  
 Met Gln Gly Leu Val Ile Asn Pro Gly Phe Ala Phe Tyr Phe Thr Ala  
 145 150 155 160  
 Val Val Ser Leu Val Thr Gly Thr Met Phe Leu Met Trp Leu Gly Glu  
 165 170 175  
 Gln Ile Thr Glu Arg Gly Ile Gly Asn Gly Ile Ser Ile Ile Ile Phe  
 180 185 190  
 Ala Gly Ile Val Ala Gly Leu Pro Pro Ala Ile Ala His Thr Ile Glu  
 195 200 205  
 Gln Ala Arg Gln Gly Asp Leu His Phe Leu Val Leu Leu Val Ala  
 210 215 220  
 Val Leu Val Phe Ala Val Thr Phe Phe Val Val Phe Val Glu Arg Gly  
 225 230 235 240  
 Gln Arg Arg Ile Val Val Asn Tyr Ala Lys Arg Gln Gln Gly Arg Arg  
 245 250 255  
 Val Tyr Ala Ala Gln Ser Thr His Leu Pro Leu Lys Val Asn Met Ala  
 260 265 270  
 Gly Val Ile Pro Ala Ile Phe Ala Ser Ser Ile Ile Leu Phe Pro Ala

275	280	285
Thr Ile Ala Ser Trp Phe Gly Gly Gly Thr Gly Trp Asn Trp Leu Thr		
290	295	300
Thr Ile Ser Leu Tyr Leu Gln Pro Gly Gln Pro Leu Tyr Val Leu Leu		
305	310	315
Tyr Ala Ser Ala Ile Ile Phe Phe Cys Phe Phe Tyr Thr Ala Leu Val		
	325	330
Phe Asn Pro Arg Glu Thr Ala Asp Asn Leu Lys Lys Ser Gly Ala Phe		
	340	345
Val Pro Gly Ile Arg Pro Gly Glu Gln Thr Ala Lys Tyr Ile Asp Lys		
	355	360
Val Met Thr Arg Leu Thr Leu Val Gly Ala Leu Tyr Ile Thr Phe Ile		
	370	375
Cys Leu Ile Pro Glu Phe Met Arg Asp Ala Met Lys Val Pro Phe Tyr		
385	390	395
Phe Gly Gly Thr Ser Leu Leu Ile Val Val Val Val Ile Met Asp Phe		
	405	410
Met Ala Gln Val Gln Thr Leu Met Met Ser Ser Gln Tyr Glu Ser Ala		
	420	425
Leu Lys Lys Ala Asn Leu Lys Gly Tyr Gly Arg		
	435	440

<210> 313  
 <211> 144  
 <212> PRT  
 <213> E. Coli

<400> 313

Met Arg Leu Asn Thr Leu Ser Pro Ala Glu Gly Ser Lys Lys Ala Gly		
1	5	10
Lys Arg Leu Gly Arg Gly Ile Gly Ser Gly Leu Gly Lys Thr Gly Gly		
	20	25
Arg Gly His Lys Gly Gln Lys Ser Arg Ser Gly Gly Gly Val Arg Arg		
	35	40
Gly Phe Glu Gly Gly Gln Met Pro Leu Tyr Arg Arg Leu Pro Lys Phe		
	50	55
Gly Phe Thr Ser Arg Lys Ala Ala Ile Thr Ala Glu Ile Arg Leu Ser		
65	70	75
Asp Leu Ala Lys Val Glu Gly Gly Val Val Asp Leu Asn Thr Leu Lys		
	85	90
Ala Ala Asn Ile Ile Gly Ile Gln Ile Glu Phe Ala Lys Val Ile Leu		
	100	105
Ala Gly Glu Val Thr Thr Pro Val Thr Val Arg Gly Leu Arg Val Thr		
	115	120
Lys Gly Ala Arg Ala Ala Ile Glu Ala Ala Gly Gly Lys Ile Glu Glu		
	130	135
		140

<210> 314  
 <211> 59  
 <212> PRT  
 <213> E. Coli

<400> 314

Met Ala Lys Thr Ile Lys Ile Thr Gln Thr Arg Ser Ala Ile Gly Arg		
1	5	10
Leu Pro Lys His Lys Ala Thr Leu Leu Gly Leu Gly Leu Arg Arg Ile		
	20	25
Gly His Thr Val Glu Arg Glu Asp Thr Pro Ala Ile Arg Gly Met Ile		
		30

35 40 45  
 Asn Ala Val Ser Phe Met Val Lys Val Glu Glu  
 50 55

<210> 315  
 <211> 167  
 <212> PRT  
 <213> E. Coli

<400> 315  
 Met Ala His Ile Glu Lys Gln Ala Gly Glu Leu Gln Glu Lys Leu Ile  
 1 5 10 15  
 Ala Val Asn Arg Val Ser Lys Thr Val Lys Gly Gly Arg Ile Phe Ser  
 20 25 30  
 Phe Thr Ala Leu Thr Val Val Gly Asp Gly Asn Gly Arg Val Gly Phe  
 35 40 45  
 Gly Tyr Gly Lys Ala Arg Glu Val Pro Ala Ala Ile Gln Lys Ala Met  
 50 55 60  
 Glu Lys Ala Arg Arg Asn Met Ile Asn Val Ala Leu Asn Asn Gly Thr  
 65 70 75 80  
 Leu Gln His Pro Val Lys Gly Val His Thr Gly Ser Arg Val Phe Met  
 85 90 95  
 Gln Pro Ala Ser Glu Gly Thr Gly Ile Ala Gly Gly Ala Met Arg  
 100 105 110  
 Ala Val Leu Glu Val Ala Gly Val His Asn Val Leu Ala Lys Ala Tyr  
 115 120 125  
 Gly Ser Thr Asn Pro Ile Asn Val Val Arg Ala Thr Ile Asp Gly Leu  
 130 135 140  
 Glu Asn Met Asn Ser Pro Glu Met Val Ala Ala Lys Arg Gly Lys Ser  
 145 150 155 160  
 Val Glu Glu Ile Leu Gly Lys  
 165

<210> 316  
 <211> 117  
 <212> PRT  
 <213> E. Coli

<400> 316  
 Met Asp Lys Lys Ser Ala Arg Ile Arg Arg Ala Thr Arg Ala Arg Arg  
 1 5 10 15  
 Lys Leu Gln Glu Leu Gly Ala Thr Arg Leu Val Val His Arg Thr Pro  
 20 25 30  
 Arg His Ile Tyr Ala Gln Val Ile Ala Pro Asn Gly Ser Glu Val Leu  
 35 40 45  
 Val Ala Ala Ser Thr Val Glu Lys Ala Ile Ala Glu Gln Leu Lys Tyr  
 50 55 60  
 Thr Gly Asn Lys Asp Ala Ala Ala Val Gly Lys Ala Val Ala Glu  
 65 70 75 80  
 Arg Ala Leu Glu Lys Gly Ile Lys Asp Val Ser Phe Asp Arg Ser Gly  
 85 90 95  
 Phe Gln Tyr His Gly Arg Val Gln Ala Leu Ala Asp Ala Ala Arg Glu  
 100 105 110  
 Ala Gly Leu Gln Phe  
 115

<210> 317  
 <211> 177

<212> PRT  
<213> E. Coli

<400> 317

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Met Ser Arg Val Ala Lys Ala Pro Val Val Val Pro Ala Gly Val Asp
 1          5          10          15
Val Lys Ile Asn Gly Gln Val Ile Thr Ile Lys Gly Lys Asn Gly Glu
 20          25          30
Leu Thr Arg Thr Leu Asn Asp Ala Val Glu Val Lys His Ala Asp Asn
 35          40          45
Thr Leu Thr Phe Gly Pro Arg Asp Gly Tyr Ala Asp Gly Trp Ala Gln
 50          55          60
Ala Gly Thr Ala Arg Ala Leu Leu Asn Ser Met Val Ile Gly Val Thr
 65          70          75          80
Glu Gly Phe Thr Lys Lys Leu Gln Leu Val Gly Val Gly Tyr Arg Ala
 85          90          95
Ala Val Lys Gly Asn Val Ile Asn Leu Ser Leu Gly Phe Ser His Pro
 100         105         110
Val Asp His Gln Leu Pro Ala Gly Ile Thr Ala Glu Cys Pro Thr Gln
 115         120         125
Thr Glu Ile Val Leu Lys Gly Ala Asp Lys Gln Val Ile Gly Gln Val
 130         135         140
Ala Ala Asp Leu Arg Ala Tyr Arg Arg Pro Glu Pro Tyr Lys Gly Lys
 145         150         155         160
Gly Val Arg Tyr Ala Asp Glu Val Val Arg Thr Lys Glu Ala Lys Lys
 165         170         175
Lys

```

<210> 318  
<211> 130  
<212> PRT  
<213> E. Coli

<400> 318

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Met Ser Met Gln Asp Pro Ile Ala Asp Met Leu Thr Arg Ile Arg Asn
 1          5          10          15
Gly Gln Ala Ala Asn Lys Ala Ala Val Thr Met Pro Ser Ser Lys Leu
 20          25          30
Lys Val Ala Ile Ala Asn Val Leu Lys Glu Glu Gly Phe Ile Glu Asp
 35          40          45
Phe Lys Val Glu Gly Asp Thr Lys Pro Glu Leu Glu Leu Thr Leu Lys
 50          55          60
Tyr Phe Gln Gly Lys Ala Val Val Glu Ser Ile Gln Arg Val Ser Arg
 65          70          75          80
Pro Gly Leu Arg Ile Tyr Lys Arg Lys Asp Glu Leu Pro Lys Val Met
 85          90          95
Ala Gly Leu Gly Ile Ala Val Val Ser Thr Ser Lys Gly Val Met Thr
 100         105         110
Asp Arg Ala Ala Arg Gln Ala Gly Leu Gly Gly Glu Ile Ile Cys Tyr
 115         120         125
Val Ala
 130

```

<210> 319  
<211> 101  
<212> PRT  
<213> E. Coli

&lt;400&gt; 319

```

Met Ala Lys Gln Ser Met Lys Ala Arg Glu Val Lys Arg Val Ala Leu
 1          5          10          15
Ala Asp Lys Tyr Phe Ala Lys Arg Ala Glu Leu Lys Ala Ile Ile Ser
          20          25          30
Asp Val Asn Ala Ser Asp Glu Asp Arg Trp Asn Ala Val Leu Lys Leu
          35          40          45
Gln Thr Leu Pro Arg Asp Ser Ser Pro Ser Arg Gln Arg Asn Arg Cys
          50          55          60
Arg Gln Thr Gly Arg Pro His Gly Phe Leu Arg Lys Phe Gly Leu Ser
65          70          75          80
Arg Ile Lys Val Arg Glu Ala Ala Met Arg Gly Glu Ile Pro Gly Leu
          85          90          95
Lys Lys Ala Ser Trp
          100

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&lt;210&gt; 320

&lt;211&gt; 179

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 320

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Met Ala Lys Leu His Asp Tyr Tyr Lys Asp Glu Val Val Lys Lys Leu
 1          5          10          15
Met Thr Glu Phe Asn Tyr Asn Ser Val Met Gln Val Pro Arg Val Glu
          20          25          30
Lys Ile Thr Leu Asn Met Gly Val Gly Glu Ala Ile Ala Asp Lys Lys
          35          40          45
Leu Leu Asp Asn Ala Ala Ala Asp Leu Ala Ala Ile Ser Gly Gln Lys
          50          55          60
Pro Leu Ile Thr Lys Ala Arg Lys Ser Val Ala Gly Phe Lys Ile Arg
65          70          75          80
Gln Gly Tyr Pro Ile Gly Cys Lys Val Thr Leu Arg Gly Glu Arg Met
          85          90          95
Trp Glu Phe Phe Glu Arg Leu Ile Thr Ile Ala Val Pro Arg Ile Arg
          100          105          110
Asp Phe Arg Gly Leu Ser Ala Lys Ser Phe Asp Gly Arg Gly Asn Tyr
          115          120          125
Ser Met Gly Val Arg Glu Gln Ile Ile Phe Pro Glu Ile Asp Tyr Asp
          130          135          140
Lys Val Asp Arg Val Arg Gly Leu Asp Ile Thr Ile Thr Thr Thr Ala
145          150          155          160
Lys Ser Asp Glu Glu Gly Arg Ala Leu Leu Ala Ala Phe Asp Phe Pro
          165          170          175
Phe Arg Lys

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&lt;210&gt; 321Z

&lt;211&gt; 104

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 321

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Met Ala Ala Lys Ile Arg Arg Asp Asp Glu Val Ile Val Leu Thr Gly
 1          5          10          15
Lys Asp Lys Gly Lys Arg Gly Lys Val Lys Asn Val Leu Ser Ser Gly
          20          25          30

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Lys Val Ile Val Glu Gly Ile Asn Leu Val Lys Lys His Gln Lys Pro  
           35                          40                          45  
 Val Pro Ala Leu Asn Gln Pro Gly Gly Ile Val Glu Lys Glu Ala Ala  
           50                          55                          60  
 Ile Gln Val Ser Asn Val Ala Ile Phe Asn Ala Ala Thr Gly Lys Ala  
 65                          70                          75                          80  
 Asp Arg Val Gly Phe Arg Phe Glu Asp Gly Lys Lys Val Arg Phe Phe  
                           85                          90                          95  
 Lys Ser Asn Ser Glu Thr Ile Lys  
                           100

<210> 322  
 <211> 123  
 <212> PRT  
 <213> E. Coli

<400> 322  
 Met Ile Gln Glu Gln Thr Met Leu Asn Val Ala Asp Asn Ser Gly Ala  
   1                          5                          10                          15  
 Arg Arg Val Met Cys Ile Lys Val Leu Gly Gly Ser His Arg Arg Tyr  
           20                          25                          30  
 Ala Gly Val Gly Asp Ile Ile Lys Ile Thr Ile Lys Glu Ala Ile Pro  
           35                          40                          45  
 Arg Gly Lys Val Lys Lys Gly Asp Val Leu Lys Ala Val Val Val Arg  
           50                          55                          60  
 Thr Lys Lys Gly Val Arg Arg Pro Asp Gly Ser Val Ile Arg Phe Asp  
 65                          70                          75                          80  
 Gly Asn Ala Cys Val Leu Leu Asn Asn Asn Ser Glu Gln Pro Ile Gly  
                           85                          90                          95  
 Thr Arg Ile Phe Gly Pro Val Thr Arg Glu Leu Arg Ser Glu Lys Phe  
                           100                          105                          110  
 Met Lys Ile Ile Ser Leu Ala Pro Glu Val Leu  
           115                          120

<210> 323  
 <211> 188  
 <212> PRT  
 <213> E. Coli

<400> 323  
 Met Phe Lys Gly Gln Lys Thr Leu Ala Ala Leu Ala Val Ser Leu Leu  
   1                          5                          10                          15  
 Phe Thr Ala Pro Val Tyr Ala Ala Asp Glu Gly Ser Gly Glu Ile His  
           20                          25                          30  
 Phe Lys Gly Glu Val Ile Glu Ala Pro Cys Glu Ile His Pro Glu Asp  
           35                          40                          45  
 Ile Asp Lys Asn Ile Asp Leu Gly Gln Val Thr Thr Thr His Ile Asn  
           50                          55                          60  
 Arg Glu His His Ser Asn Lys Val Ala Val Asp Ile Arg Leu Ile Asn  
 65                          70                          75                          80  
 Cys Asp Leu Pro Ala Ser Asp Asn Gly Ser Gly Met Pro Val Ser Lys  
                           85                          90                          95  
 Val Gly Val Thr Phe Asp Ser Thr Ala Lys Thr Thr Gly Ala Thr Pro  
           100                          105                          110  
 Leu Leu Ser Asn Thr Ser Ala Gly Glu Ala Thr Gly Val Gly Val Arg  
           115                          120                          125  
 Leu Met Asp Lys Asn Asp Gly Asn Ile Val Leu Gly Ser Ala Ala Pro  
           130                          135                          140  
 Asp Leu Asp Leu Asp Ala Ser Ser Ser Glu Gln Thr Leu Asn Phe Phe

145 150 155 160  
 Ala Trp Met Glu Gln Ile Asp Asn Ala Val Asp Val Thr Ala Gly Glu  
 165 170 175  
 Val Thr Ala Asn Ala Thr Tyr Val Leu Asp Tyr Lys  
 180 185

<210> 324  
 <211> 427  
 <212> PRT  
 <213> E. Coli

<400> 324  
 Met Ala Asp Thr Lys Ala Lys Leu Thr Leu Asn Gly Asp Thr Ala Val  
 1 5 10 15  
 Glu Leu Asp Val Leu Lys Gly Thr Leu Gly Gln Asp Val Ile Asp Ile  
 20 25 30  
 Arg Thr Leu Gly Ser Lys Gly Val Phe Thr Phe Asp Pro Gly Phe Thr  
 35 40 45  
 Ser Thr Ala Ser Cys Glu Ser Lys Ile Thr Phe Ile Asp Gly Asp Glu  
 50 55 60  
 Gly Ile Leu Leu His Arg Gly Phe Pro Ile Asp Gln Leu Ala Thr Asp  
 65 70 75 80  
 Ser Asn Tyr Leu Glu Val Cys Tyr Ile Leu Leu Asn Gly Glu Lys Pro  
 85 90 95  
 Thr Gln Glu Gln Tyr Asp Glu Phe Lys Thr Thr Val Thr Arg His Thr  
 100 105 110  
 Met Ile His Glu Gln Ile Thr Arg Leu Phe His Ala Phe Arg Arg Asp  
 115 120 125  
 Ser His Pro Met Ala Val Met Cys Gly Ile Thr Gly Ala Leu Ala Ala  
 130 135 140  
 Phe Tyr His Asp Ser Leu Asp Val Asn Asn Pro Arg His Arg Glu Ile  
 145 150 155 160  
 Ala Ala Phe Arg Leu Leu Ser Lys Met Pro Thr Met Ala Ala Met Cys  
 165 170 175  
 Tyr Lys Tyr Ser Ile Gly Gln Pro Phe Val Tyr Pro Arg Asn Asp Leu  
 180 185 190  
 Ser Tyr Ala Gly Asn Phe Leu Asn Met Met Phe Ser Thr Pro Cys Glu  
 195 200 205  
 Pro Tyr Glu Val Asn Pro Ile Leu Glu Arg Ala Met Asp Arg Ile Leu  
 210 215 220  
 Ile Leu His Ala Asp His Glu Gln Asn Ala Ser Thr Ser Thr Val Arg  
 225 230 235 240  
 Thr Ala Gly Ser Ser Gly Ala Asn Pro Phe Ala Cys Ile Ala Ala Gly  
 245 250 255  
 Ile Ala Ser Leu Trp Gly Pro Ala His Gly Gly Ala Asn Glu Ala Ala  
 260 265 270  
 Leu Lys Met Leu Glu Glu Ile Ser Ser Val Lys His Ile Pro Glu Phe  
 275 280 285  
 Val Arg Arg Ala Lys Asp Lys Asn Asp Ser Phe Arg Leu Met Gly Phe  
 290 295 300  
 Gly His Arg Val Tyr Lys Asn Tyr Asp Pro Arg Ala Thr Val Met Arg  
 305 310 315 320  
 Glu Thr Cys His Glu Val Leu Lys Glu Leu Gly Thr Lys Asp Asp Leu  
 325 330 335  
 Leu Glu Val Ala Met Glu Leu Glu Asn Ile Ala Leu Asn Asp Pro Tyr  
 340 345 350  
 Phe Ile Glu Lys Lys Leu Tyr Pro Asn Val Asp Phe Tyr Ser Gly Ile  
 355 360 365  
 Ile Leu Lys Ala Met Gly Ile Pro Ser Ser Met Phe Thr Val Ile Phe  
 370 375 380

Ala Met Ala Arg Thr Val Gly Trp Ile Ala His Trp Ser Glu Met His  
 385 390 395 400  
 Ser Asp Gly Met Lys Ile Ala Arg Pro Arg Gln Leu Tyr Thr Gly Tyr  
 405 410 415  
 Glu Lys Arg Asp Phe Lys Ser Asp Ile Lys Arg  
 420 425

<210> 325  
 <211> 477  
 <212> PRT  
 <213> E. Coli

<400> 325  
 Met Lys Val Thr Leu Pro Glu Phe Glu Arg Ala Gly Val Met Val Val  
 1 5 10 15  
 Gly Asp Val Met Leu Asp Arg Tyr Trp Tyr Gly Pro Thr Ser Arg Ile  
 20 25 30  
 Ser Pro Glu Ala Pro Val Pro Val Lys Val Asn Thr Ile Glu Glu  
 35 40 45  
 Arg Pro Gly Gly Ala Ala Asn Val Ala Met Asn Ile Ala Ser Leu Gly  
 50 55 60  
 Ala Asn Ala Arg Leu Val Gly Leu Thr Gly Ile Asp Asp Ala Ala Arg  
 65 70 75 80  
 Ala Leu Ser Lys Ser Leu Ala Asp Val Asn Val Lys Cys Asp Phe Val  
 85 90 95  
 Ser Val Pro Thr His Pro Thr Ile Thr Lys Leu Arg Val Leu Ser Arg  
 100 105 110  
 Asn Gln Gln Leu Ile Arg Leu Asp Phe Glu Glu Gly Phe Glu Gly Val  
 115 120 125  
 Asp Pro Gln Pro Leu His Glu Arg Ile Asn Gln Ala Leu Ser Ser Ile  
 130 135 140  
 Gly Ala Leu Val Leu Ser Asp Tyr Ala Lys Gly Ala Leu Ala Ser Val  
 145 150 155 160  
 Gln Gln Met Ile Gln Leu Ala Arg Lys Ala Gly Val Pro Val Leu Ile  
 165 170 175  
 Asp Pro Lys Gly Thr Asp Phe Glu Arg Tyr Arg Gly Ala Thr Leu Leu  
 180 185 190  
 Thr Pro Asn Leu Ser Glu Phe Glu Ala Val Val Gly Lys Cys Lys Thr  
 195 200 205  
 Glu Glu Glu Ile Val Glu Arg Gly Met Lys Leu Ile Ala Asp Tyr Glu  
 210 215 220  
 Leu Ser Ala Leu Leu Val Thr Arg Ser Glu Gln Gly Met Ser Leu Leu  
 225 230 235 240  
 Gln Pro Gly Lys Ala Pro Leu His Met Pro Thr Gln Ala Gln Glu Val  
 245 250 255  
 Tyr Asp Val Thr Gly Ala Gly Asp Thr Val Ile Gly Val Leu Ala Ala  
 260 265 270  
 Thr Leu Ala Ala Gly Asn Ser Leu Glu Glu Ala Cys Phe Phe Ala Asn  
 275 280 285  
 Ala Ala Ala Gly Val Val Val Gly Lys Leu Gly Thr Ser Thr Val Ser  
 290 295 300  
 Pro Ile Glu Leu Glu Asn Ala Val Arg Gly Arg Ala Asp Thr Gly Phe  
 305 310 315 320  
 Gly Val Met Thr Glu Glu Glu Leu Lys Leu Ala Val Ala Ala Ala Arg  
 325 330 335  
 Lys Arg Gly Glu Lys Val Val Met Thr Asn Gly Val Phe Asp Ile Leu  
 340 345 350  
 His Ala Gly His Val Ser Tyr Leu Ala Asn Ala Arg Lys Leu Gly Asp  
 355 360 365  
 Arg Leu Ile Val Ala Val Asn Ser Asp Ala Ser Thr Lys Arg Leu Lys



370	375	380
Gly Asp Ser Arg Pro Val Asn Pro Leu Glu Gln Arg Met Ile Val Leu		
385	390	395
Gly Ala Leu Glu Ala Val Asp Trp Val Val Ser Phe Glu Glu Asp Thr		400
	405	410
Pro Gln Arg Leu Ile Ala Gly Ile Leu Pro Asp Leu Leu Val Lys Gly		415
	420	425
Gly Asp Tyr Lys Pro Glu Glu Ile Ala Gly Ser Lys Glu Val Trp Ala		430
	435	440
Asn Gly Gly Glu Val Leu Val Leu Asn Phe Glu Asp Gly Cys Ser Thr		445
	450	455
Thr Asn Ile Ile Lys Lys Ile Gln Gln Asp Lys Lys Gly		460
465	470	475

<210> 326  
 <211> 946  
 <212> PRT  
 <213> E. Coli

<400> 326

Met Lys Pro Leu Ser Ser Pro Leu Gln Gln Tyr Trp Gln Thr Val Val		
1	5	10
Glu Arg Leu Pro Glu Pro Leu Ala Glu Glu Ser Leu Ser Ala Gln Ala		15
	20	25
Lys Ser Val Leu Thr Phe Ser Asp Phe Val Gln Asp Ser Val Ile Ala		30
	35	40
His Pro Glu Trp Leu Thr Glu Leu Glu Ser Gln Pro Pro Gln Ala Asp		45
	50	55
Glu Trp Gln His Tyr Ala Ala Trp Leu Gln Glu Ala Leu Cys Asn Val		60
	65	70
Ser Asp Glu Ala Gly Leu Met Arg Glu Leu Arg Leu Phe Arg Arg Arg		75
	85	90
Ile Met Val Arg Ile Ala Trp Ala Gln Thr Leu Ala Leu Val Thr Glu		95
	100	105
Glu Ser Ile Leu Gln Gln Leu Ser Tyr Leu Ala Glu Thr Leu Ile Val		110
	115	120
Ala Ala Arg Asp Trp Leu Tyr Asp Ala Cys Cys Arg Glu Trp Gly Thr		125
	130	135
Pro Cys Asn Ala Gln Gly Glu Ala Gln Pro Leu Leu Ile Leu Gly Met		140
	145	150
Gly Lys Leu Gly Gly Gly Glu Leu Asn Phe Ser Ser Asp Ile Asp Leu		155
	165	170
Ile Phe Ala Trp Pro Glu His Gly Cys Thr Gln Gly Gly Arg Arg Glu		175
	180	185
Leu Asp Asn Ala Gln Phe Phe Thr Arg Met Gly Gln Arg Leu Ile Lys		190
	195	200
Val Leu Asp Gln Pro Thr Gln Asp Gly Phe Val Tyr Arg Val Asp Met		205
	210	215
Arg Leu Arg Pro Phe Gly Glu Ser Gly Pro Leu Val Leu Ser Phe Ala		220
	225	230
Ala Leu Glu Asp Tyr Tyr Gln Glu Gln Gly Arg Asp Trp Glu Arg Tyr		235
	245	250
Ala Met Val Lys Ala Arg Ile Met Gly Asp Ser Glu Gly Val Tyr Ala		255
	260	265
Asn Glu Leu Arg Ala Met Leu Arg Pro Phe Val Phe Arg Arg Tyr Ile		270
	275	280
Asp Phe Ser Val Ile Gln Ser Leu Arg Asn Met Lys Gly Met Ile Ala		285
	290	295
Arg Glu Val Arg Arg Arg Gly Leu Thr Asp Asn Ile Lys Leu Gly Ala		300
	305	310
		315
		320

Gly Gly Ile Arg Glu Ile Glu Phe Ile Val Gln Val Phe Gln Leu Ile  
 325 330 335  
 Arg Gly Gly Arg Glu Pro Ser Leu Gln Ser Arg Ser Leu Leu Pro Thr  
 340 345 350  
 Leu Ser Ala Ile Ala Glu Leu His Leu Leu Ser Glu Asn Asp Ala Glu  
 355 360 365  
 Gln Leu Arg Val Ala Tyr Leu Phe Leu Arg Arg Leu Glu Asn Leu Leu  
 370 375 380  
 Gln Ser Ile Asn Asp Glu Gln Thr Gln Thr Leu Pro Ser Asp Glu Leu  
 385 390 395 400  
 Asn Arg Ala Arg Leu Ala Trp Ala Met Asp Phe Ala Asp Trp Pro Gln  
 405 410 415  
 Leu Thr Gly Ala Leu Thr Ala His Met Thr Asn Val Arg Arg Val Phe  
 420 425 430  
 Asn Glu Leu Ile Gly Asp Asp Glu Ser Glu Thr Gln Glu Glu Ser Leu  
 435 440 445  
 Ser Glu Gln Trp Arg Glu Leu Trp Gln Asp Ala Leu Gln Glu Asp Asp  
 450 455 460  
 Thr Thr Pro Val Leu Ala His Leu Ser Glu Asp Arg Lys Gln Val  
 465 470 475 480  
 Leu Thr Leu Ile Ala Asp Phe Arg Lys Glu Leu Asp Lys Arg Thr Ile  
 485 490 495  
 Gly Pro Arg Gly Arg Gln Val Leu Asp His Leu Met Pro His Leu Leu  
 500 505 510  
 Ser Asp Val Cys Ala Arg Glu Asp Ala Ala Val Thr Leu Ser Arg Ile  
 515 520 525  
 Thr Ala Leu Leu Val Gly Ile Val Thr Arg Thr Thr Tyr Leu Glu Leu  
 530 535 540  
 Leu Ser Glu Phe Pro Ala Ala Leu Lys His Leu Ile Ser Leu Cys Ala  
 545 550 555 560  
 Ala Ser Pro Met Ile Ala Ser Gln Leu Ala Arg Tyr Pro Leu Leu Leu  
 565 570 575  
 Asp Glu Leu Leu Asp Pro Asn Thr Leu Tyr Gln Pro Thr Ala Thr Asp  
 580 585 590  
 Ala Tyr Arg Asp Glu Leu Arg Gln Tyr Leu Leu Arg Val Pro Glu Asp  
 595 600 605  
 Asp Glu Glu Gln Gln Leu Glu Ala Leu Arg Gln Phe Lys Gln Ala Gln  
 610 615 620  
 Leu Leu Arg Ile Ala Ala Ala Asp Ile Ala Gly Thr Leu Pro Val Met  
 625 630 635 640  
 Lys Val Ser Asp His Leu Thr Trp Leu Ala Glu Ala Met Ile Asp Ala  
 645 650 655  
 Val Val Gln Gln Ala Trp Val Gln Met Val Ala Arg Tyr Gly Lys Pro  
 660 665 670  
 Asn His Leu Asn Glu Arg Glu Gly Arg Gly Phe Ala Val Val Gly Tyr  
 675 680 685  
 Gly Lys Leu Gly Gly Trp Glu Leu Gly Tyr Ser Ser Asp Leu Asp Leu  
 690 695 700  
 Ile Phe Leu His Asp Cys Pro Met Asp Ala Met Thr Asp Gly Glu Arg  
 705 710 715 720  
 Glu Ile Asp Gly Arg Gln Phe Tyr Leu Arg Leu Ala Gln Arg Ile Met  
 725 730 735  
 His Leu Phe Ser Thr Arg Thr Ser Ser Gly Ile Leu Tyr Glu Val Asp  
 740 745 750  
 Ala Arg Leu Arg Pro Ser Gly Ala Ala Gly Met Leu Val Thr Ser Ala  
 755 760 765  
 Glu Ala Phe Ala Asp Tyr Gln Lys Asn Glu Ala Trp Thr Trp Glu His  
 770 775 780  
 Gln Ala Leu Val Arg Ala Arg Val Val Tyr Gly Asp Pro Gln Leu Thr  
 785 790 795 800  
 Ala His Phe Asp Ala Val Arg Arg Glu Ile Met Thr Leu Pro Arg Glu

				805					810					815					
Gly	Lys	Thr	Leu	Gln	Thr	Glu	Val	Arg	Glu	Met	Arg	Glu	Lys	Met	Arg				
			820					825					830						
Ala	His	Leu	Gly	Asn	Lys	His	Arg	Asp	Arg	Phe	Asp	Ile	Lys	Ala	Asp				
		835					840					845							
Glu	Gly	Gly	Ile	Thr	Asp	Ile	Glu	Phe	Ile	Thr	Gln	Tyr	Leu	Val	Leu				
	850					855					860								
Arg	Tyr	Ala	His	Glu	Lys	Pro	Lys	Leu	Thr	Arg	Trp	Ser	Asp	Asn	Val				
865					870					875					880				
Arg	Ile	Leu	Glu	Leu	Leu	Ala	Gln	Asn	Asp	Ile	Met	Glu	Glu	Gln	Glu				
			885					890						895					
Ala	Met	Ala	Leu	Thr	Arg	Ala	Tyr	Thr	Thr	Leu	Arg	Asp	Glu	Leu	His				
		900						905					910						
His	Leu	Ala	Leu	Gln	Glu	Leu	Pro	Gly	His	Val	Ser	Glu	Asp	Cys	Phe				
	915						920					925							
Thr	Ala	Glu	Arg	Glu	Leu	Val	Arg	Ala	Ser	Trp	Gln	Lys	Trp	Leu	Val				
	930					935					940								
Glu	Glu																		
945																			

<210> 327  
 <211> 433  
 <212> PRT  
 <213> E. Coli

<400> 327

Met	Ala	Gln	Glu	Ile	Glu	Leu	Lys	Phe	Ile	Val	Asn	His	Ser	Ala	Val				
1				5					10					15					
Glu	Ala	Leu	Arg	Asp	His	Leu	Asn	Thr	Leu	Gly	Gly	Glu	His	His	Asp				
		20						25					30						
Pro	Val	Gln	Leu	Leu	Asn	Ile	Tyr	Glu	Thr	Pro	Asp	Asn	Trp	Leu					
	35					40					45								
Arg	Gly	His	Asp	Met	Gly	Leu	Arg	Ile	Arg	Gly	Glu	Asn	Gly	Arg	Tyr				
	50					55					60								
Glu	Met	Thr	Met	Lys	Val	Ala	Gly	Arg	Val	Thr	Gly	Gly	Leu	His	Gln				
65				70					75					80					
Arg	Pro	Glu	Tyr	Asn	Val	Ala	Leu	Ser	Glu	Pro	Thr	Leu	Asp	Leu	Ala				
			85					90					95						
Gln	Leu	Pro	Thr	Glu	Val	Trp	Pro	Asn	Gly	Glu	Leu	Pro	Ala	Asp	Leu				
		100						105					110						
Ala	Ser	Arg	Val	Gln	Pro	Leu	Phe	Ser	Thr	Asp	Phe	Tyr	Arg	Glu	Lys				
	115						120					125							
Trp	Leu	Val	Ala	Val	Asp	Gly	Ser	Gln	Ile	Glu	Ile	Ala	Leu	Asp	Gln				
	130					135					140								
Gly	Glu	Val	Lys	Ala	Gly	Glu	Phe	Ala	Glu	Pro	Ile	Cys	Glu	Leu	Glu				
145					150				155					160					
Leu	Glu	Leu	Leu	Ser	Gly	Asp	Thr	Arg	Ala	Val	Leu	Lys	Leu	Ala	Asn				
			165					170					175						
Gln	Leu	Val	Ser	Gln	Thr	Gly	Leu	Arg	Gln	Gly	Ser	Leu	Ser	Lys	Ala				
		180						185					190						
Ala	Arg	Gly	Tyr	His	Leu	Ala	Gln	Gly	Asn	Pro	Ala	Arg	Glu	Ile	Lys				
	195						200					205							
Pro	Thr	Thr	Ile	Leu	His	Val	Ala	Ala	Lys	Ala	Asp	Val	Glu	Gln	Gly				
	210					215					220								
Leu	Glu	Ala	Ala	Leu	Glu	Leu	Ala	Leu	Ala	Gln	Trp	Gln	Tyr	His	Glu				
225				230					235					240					
Glu	Leu	Trp	Val	Arg	Gly	Asn	Asp	Ala	Ala	Lys	Glu	Gln	Val	Leu	Ala				
			245					250					255						
Ala	Ile	Ser	Leu	Val	Arg	His	Thr	Leu	Met	Leu	Phe	Gly	Gly	Ile	Val				

260 265 270  
 Pro Arg Lys Ala Ser Thr His Leu Arg Asp Leu Leu Thr Gln Cys Glu  
 275 280 285  
 Ala Thr Ile Ala Ser Ala Val Ser Ala Val Thr Ala Val Tyr Ser Thr  
 290 295 300  
 Glu Thr Ala Met Ala Lys Leu Ala Leu Thr Glu Trp Leu Val Ser Lys  
 305 310 315 320  
 Ala Trp Gln Pro Phe Leu Asp Ala Lys Ala Gln Gly Lys Ile Ser Asp  
 325 330 335  
 Ser Phe Lys Arg Phe Ala Asp Ile His Leu Ser Arg His Ala Ala Glu  
 340 345 350  
 Leu Lys Ser Val Phe Cys Gln Pro Leu Gly Asp Arg Tyr Arg Asp Gln  
 355 360 365  
 Leu Pro Arg Leu Thr Arg Asp Ile Asp Ser Ile Leu Leu Leu Ala Gly  
 370 375 380  
 Tyr Tyr Asp Pro Val Val Ala Gln Ala Trp Leu Glu Asn Trp Gln Gly  
 385 390 395 400  
 Leu His His Ala Ile Ala Thr Gly Gln Arg Ile Glu Ile Glu His Phe  
 405 410 415  
 Arg Asn Glu Ala Asn Asn Gln Glu Pro Phe Trp Leu His Ser Gly Lys  
 420 425 430  
 Arg

<210> 328  
 <211> 70  
 <212> PRT  
 <213> E. Coli

<400> 328  
 Met Ser Gly Lys Met Thr Gly Ile Val Lys Trp Phe Asn Ala Asp Lys  
 1 5 10 15  
 Gly Phe Gly Phe Ile Thr Pro Asp Asp Gly Ser Lys Asp Val Phe Val  
 20 25 30  
 His Phe Ser Ala Ile Gln Asn Asp Gly Tyr Lys Ser Leu Asp Glu Gly  
 35 40 45  
 Gln Lys Val Ser Phe Thr Ile Glu Ser Gly Ala Lys Gly Pro Ala Ala  
 50 55 60  
 Gly Asn Val Thr Ser Leu  
 65 70

<210> 329  
 <211> 523  
 <212> PRT  
 <213> E. Coli

<400> 329  
 Met Arg Asp Ile Val Asp Pro Val Phe Ser Ile Gly Ile Ser Ser Leu  
 1 5 10 15  
 Trp Asp Glu Leu Arg His Met Pro Ala Gly Gly Val Trp Trp Phe Asn  
 20 25 30  
 Val Asp Arg His Glu Asp Ala Ile Ser Leu Ala Asn Gln Thr Ile Ala  
 35 40 45  
 Ser Gln Ala Glu Thr Ala His Val Ala Val Ile Ser Met Asp Ser Asp  
 50 55 60  
 Pro Ala Lys Ile Phe Gln Leu Asp Asp Ser Gln Gly Pro Glu Lys Ile  
 65 70 75 80

Lys Leu Phe Ser Met Leu Asn His Glu Lys Gly Leu Tyr Tyr Leu Thr  
 85 90 95  
 Arg Asp Leu Gln Cys Ser Ile Asp Pro His Asn Tyr Leu Phe Ile Leu  
 100 105 110  
 Val Cys Ala Asn Asn Ala Trp Gln Asn Ile Pro Ala Glu Arg Leu Arg  
 115 120 125  
 Ser Trp Leu Asp Lys Met Asn Lys Trp Ser Arg Leu Asn His Cys Ser  
 130 135 140  
 Leu Leu Val Ile Asn Pro Gly Asn Asn Asn Asp Lys Gln Phe Ser Leu  
 145 150 155 160  
 Leu Leu Glu Glu Tyr Arg Ser Leu Phe Gly Leu Ala Ser Leu Arg Phe  
 165 170 175  
 Gln Gly Asp Gln His Leu Leu Asp Ile Ala Phe Trp Cys Asn Glu Lys  
 180 185 190  
 Gly Val Ser Ala Arg Gln Gln Leu Ser Val Gln Gln Gln Asn Gly Ile  
 195 200 205  
 Trp Thr Leu Val Gln Ser Glu Glu Ala Glu Ile Gln Pro Arg Ser Asp  
 210 215 220  
 Glu Lys Arg Ile Leu Ser Asn Val Ala Val Leu Glu Gly Ala Pro Pro  
 225 230 235 240  
 Leu Ser Glu His Trp Gln Leu Phe Asn Asn Asn Glu Val Leu Phe Asn  
 245 250 255  
 Glu Ala Arg Thr Ala Gln Ala Ala Thr Val Val Phe Ser Leu Gln Gln  
 260 265 270  
 Asn Ala Gln Ile Glu Pro Leu Ala Arg Ser Ile His Thr Leu Arg Arg  
 275 280 285  
 Gln Arg Gly Ser Ala Met Lys Ile Leu Val Arg Glu Asn Thr Ala Ser  
 290 295 300  
 Leu Arg Ala Thr Asp Glu Arg Leu Leu Leu Ala Cys Gly Ala Asn Met  
 305 310 315 320  
 Val Ile Pro Trp Asn Ala Pro Leu Ser Arg Cys Leu Thr Met Ile Glu  
 325 330 335  
 Ser Val Gln Gly Gln Lys Phe Ser Arg Tyr Val Pro Glu Asp Ile Thr  
 340 345 350  
 Thr Leu Leu Ser Met Thr Gln Pro Leu Lys Leu Arg Gly Phe Gln Lys  
 355 360 365  
 Trp Asp Val Phe Cys Asn Ala Val Asn Asn Met Met Asn Asn Pro Leu  
 370 375 380  
 Leu Pro Ala His Gly Lys Gly Val Leu Val Ala Leu Arg Pro Val Pro  
 385 390 395 400  
 Gly Ile Arg Val Glu Gln Ala Leu Thr Leu Cys Arg Pro Asn Arg Thr  
 405 410 415  
 Gly Asp Ile Met Thr Ile Gly Gly Asn Arg Leu Val Leu Phe Leu Ser  
 420 425 430  
 Phe Cys Arg Ile Asn Asp Leu Asp Thr Ala Leu Asn His Ile Phe Pro  
 435 440 445  
 Leu Pro Thr Gly Asp Ile Phe Ser Asn Arg Met Val Trp Phe Glu Asp  
 450 455 460  
 Asp Gln Ile Ser Ala Glu Leu Val Gln Met Arg Leu Leu Ala Pro Glu  
 465 470 475 480  
 Gln Trp Gly Met Pro Leu Pro Leu Thr Gln Ser Ser Lys Pro Val Ile  
 485 490 495  
 Asn Ala Glu His Asp Gly Arg His Trp Arg Arg Ile Pro Glu Pro Met  
 500 505 510  
 Arg Leu Leu Asp Asp Ala Val Glu Arg Ser Ser  
 515 520

&lt;210&gt; 330

&lt;211&gt; 62

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 330

Met	Thr	Ile	Ser	Asp	Ile	Ile	Glu	Ile	Ile	Val	Val	Cys	Ala	Leu	Ile
1				5					10					15	
Phe	Phe	Pro	Leu	Gly	Tyr	Leu	Ala	Arg	His	Ser	Leu	Arg	Arg	Ile	Arg
			20					25					30		
Asp	Thr	Leu	Arg	Leu	Phe	Phe	Ala	Lys	Pro	Arg	Tyr	Val	Lys	Pro	Ala
		35					40					45			
Gly	Thr	Leu	Arg	Arg	Thr	Glu	Lys	Ala	Arg	Ala	Thr	Lys	Lys		
	50					55					60				

&lt;210&gt; 331

&lt;211&gt; 559

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 331

Met	Thr	Gln	Phe		Gln	Asn	Thr	Ala	Met	Pro	Ser	Ser	Leu	Trp	Gln
1				5					10					15	
Tyr	Trp	Arg	Gly	Leu	Ser	Gly	Trp	Asn	Phe	Tyr	Phe	Leu	Val	Lys	Phe
			20					25					30		
Gly	Leu	Leu	Trp	Ala	Gly	Tyr	Leu	Asn	Phe	His	Pro	Leu	Leu	Asn	Leu
		35					40					45			
Val	Phe	Ala	Ala	Phe	Leu	Leu	Met	Pro	Leu	Pro	Arg	Tyr	Ser	Leu	His
	50				55					60					
Arg	Leu	Arg	His	Trp	Ile	Ala	Leu	Pro	Ile	Gly	Phe	Ala	Leu	Phe	Trp
65				70					75					80	
His	Asp	Thr	Trp	Leu	Pro	Gly	Pro	Glu	Ser	Ile	Met	Ser	Gln	Gly	Ser
			85					90						95	
Gln	Val	Ala	Gly	Phe	Ser	Thr	Asp	Tyr	Leu	Ile	Asp	Leu	Val	Thr	Arg
		100						105					110		
Phe	Ile	Asn	Trp	Gln	Met	Ile	Gly	Ala	Ile	Phe	Val	Leu	Leu	Val	Ala
		115					120					125			
Trp	Leu	Phe	Leu	Ser	Gln	Trp	Ile	Arg	Ile	Thr	Val	Phe	Val	Val	Ala
		130				135					140				
Ile	Leu	Leu	Trp	Leu	Asn	Val	Leu	Thr	Leu	Ala	Gly	Pro	Ser	Phe	Ser
145				150					155						160
Leu	Trp	Pro	Ala	Gly	Gln	Pro	Thr	Thr	Thr	Val	Thr	Thr	Thr	Gly	Gly
			165					170						175	
Asn	Ala	Ala	Ala	Thr	Val	Ala	Ala	Thr	Gly	Gly	Ala	Pro	Val	Val	Gly
		180						185					190		
Asp	Met	Pro	Ala	Gln	Thr	Ala	Pro	Pro	Thr	Thr	Ala	Asn	Leu	Asn	Ala
	195						200					205			
Trp	Leu	Asn	Asn	Phe	Tyr	Asn	Ala	Glu	Ala	Lys	Arg	Lys	Ser	Thr	Phe
	210					215					220				
Pro	Ser	Ser	Leu	Pro	Ala	Asp	Ala	Gln	Pro	Phe	Glu	Leu	Leu	Val	Ile
225				230						235					240
Asn	Ile	Cys	Ser	Leu	Ser	Trp	Ser	Asp	Ile	Glu	Ala	Ala	Gly	Leu	Met
			245					250						255	
Ser	His	Pro	Leu	Trp	Ser	His	Phe	Asp	Ile	Glu	Phe	Lys	Asn	Phe	Asn
		260					265						270		
Ser	Ala	Thr	Ser	Tyr	Ser	Gly	Pro	Ala	Ala	Ile	Arg	Leu	Leu	Arg	Ala
		275					280						285		
Ser	Cys	Gly	Gln	Thr	Ser	His	Thr	Asn	Leu	Tyr	Gln	Pro	Ala	Asn	Asn
	290					295					300				
Asp	Cys	Tyr	Leu	Phe	Asp	Asn	Leu	Ser	Lys	Leu	Gly	Phe	Thr	Gln	His
305				310						315					320
Leu	Met	Met	Gly	His	Asn	Gly	Gln	Phe	Gly	Gly	Phe	Leu	Lys	Glu	Val
			325						330					335	

Arg Glu Asn Gly Gly Met Gln Ser Glu Leu Met Asp Gln Thr Asn Leu  
 340 345 350  
 Pro Val Ile Leu Leu Gly Phe Asp Gly Ser Pro Val Tyr Asp Asp Thr  
 355 360 365  
 Ala Val Leu Asn Arg Trp Leu Asp Val Thr Glu Lys Asp Lys Asn Ser  
 370 375 380  
 Arg Ser Ala Thr Phe Tyr Asn Thr Leu Pro Leu His Asp Gly Asn His  
 385 390 395 400  
 Tyr Pro Gly Val Ser Lys Thr Ala Asp Tyr Lys Ala Arg Ala Gln Lys  
 405 410 415  
 Phe Phe Asp Glu Leu Asp Ala Phe Phe Thr Glu Leu Glu Lys Ser Gly  
 420 425 430  
 Arg Lys Val Met Val Val Val Val Pro Glu His Gly Gly Ala Leu Lys  
 435 440 445  
 Gly Asp Arg Met Gln Val Ser Gly Leu Arg Asp Ile Pro Ser Pro Ser  
 450 455 460  
 Ile Thr Asp Val Pro Val Gly Val Lys Phe Phe Gly Met Lys Ala Pro  
 465 470 475 480  
 His Gln Gly Ala Pro Ile Val Ile Glu Gln Pro Ser Ser Phe Leu Ala  
 485 490 495  
 Ile Ser Asp Leu Val Val Arg Val Leu Asp Gly Lys Ile Phe Thr Glu  
 500 505 510  
 Asp Asn Val Asp Trp Lys Lys Leu Thr Ser Gly Leu Pro Gln Thr Ala  
 515 520 525  
 Pro Val Ser Glu Asn Ser Asn Ala Val Val Ile Gln Tyr Gln Asp Lys  
 530 535 540  
 Pro Tyr Val Arg Leu Asn Gly Gly Asp Trp Val Pro Tyr Pro Gln  
 545 550 555

<210> 332  
 <211> 127  
 <212> PRT  
 <213> E. Coli

<400> 332  
 Met Glu Gly Ser Arg Met Lys Tyr Arg Ile Ala Leu Ala Val Ser Leu  
 1 5 10 15  
 Phe Ala Leu Ser Ala Gly Ser Tyr Ala Thr Thr Leu Cys Gln Glu Lys  
 20 25 30  
 Glu Gln Asn Ile Leu Lys Glu Ile Ser Tyr Ala Glu Lys His Gln Asn  
 35 40 45  
 Gln Asn Arg Ile Asp Gly Leu Asn Lys Ala Leu Ser Glu Val Arg Ala  
 50 55 60  
 Asn Cys Ser Asp Ser Gln Leu Arg Ala Asp His Gln Lys Lys Ile Ala  
 65 70 75 80  
 Lys Gln Lys Asp Glu Val Ala Glu Arg Gln Gln Asp Leu Ala Glu Ala  
 85 90 95  
 Lys Gln Lys Gly Asp Ala Asp Lys Ile Ala Lys Arg Glu Arg Lys Leu  
 100 105 110  
 Ala Glu Ala Gln Glu Glu Leu Lys Lys Leu Glu Ala Arg Asp Tyr  
 115 120 125

<210> 333  
 <211> 101  
 <212> PRT  
 <213> E. Coli

<400> 333  
 Met Ser Lys Glu His Thr Thr Glu His Leu Arg Ala Glu Leu Lys Ser

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1           5           10           15
Leu Ser Asp Thr Leu Glu Glu Val Leu Ser Ser Ser Gly Glu Lys Ser
20
Lys Glu Glu Leu Ser Lys Ile Arg Ser Lys Ala Glu Gln Ala Leu Lys
35
Gln Ser Arg Tyr Arg Leu Gly Glu Thr Gly Asp Ala Ile Ala Lys Gln
50
Thr Arg Val Ala Ala Ala Arg Ala Asp Glu Tyr Val Arg Glu Asn Pro
65
Trp Thr Gly Val Gly Ile Gly Ala Ala Ile Gly Val Val Leu Gly Val
85
Leu Leu Ser Arg Arg
100

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<210> 334
<211> 134
<212> PRT
<213> E. Coli

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<400> 334
Met Ala Asp Thr His His Ala Gln Gly Pro Gly Lys Ser Val Leu Gly
1           5           10           15
Ile Gly Gln Arg Ile Val Ser Ile Met Val Glu Met Val Glu Thr Arg
20
Leu Arg Leu Ala Val Val Glu Leu Glu Glu Glu Lys Ala Asn Leu Phe
35
Gln Leu Leu Leu Met Leu Gly Leu Thr Met Leu Phe Ala Ala Phe Gly
50
Leu Met Ser Leu Met Val Leu Ile Ile Trp Ala Val Asp Pro Gln Tyr
65
Arg Leu Asn Ala Met Ile Ala Thr Thr Val Val Leu Leu Leu Leu Ala
85
Leu Ile Gly Gly Ile Trp Thr Leu Arg Lys Ser Arg Lys Ser Thr Leu
100
Leu Arg His Thr Arg His Glu Leu Ala Asn Asp Arg Gln Leu Leu Glu
115
Glu Glu Ser Arg Glu Gln
130

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<210> 335
<211> 99
<212> PRT
<213> E. Coli

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<400> 335
Met Ser Ser Lys Val Glu Arg Glu Arg Arg Lys Ala Gln Leu Leu Ser
1           5           10           15
Gln Ile Gln Gln Gln Arg Leu Asp Leu Ser Ala Ser Arg Arg Glu Trp
20
Leu Glu Thr Thr Gly Ala Tyr Asp Arg Arg Trp Asn Met Leu Leu Ser
35
Leu Arg Ser Trp Ala Leu Val Gly Ser Ser Val Met Ala Ile Trp Thr
50
Ile Arg His Pro Asn Met Leu Val Arg Trp Ala Arg Arg Gly Phe Gly
65
Val Trp Ser Ala Trp Arg Leu Val Lys Thr Thr Leu Lys Gln Gln Gln
85
Leu Arg Gly
90

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<210> 336  
 <211> 160  
 <212> PRT  
 <213> E. Coli

<400> 336  
 Met Ile Leu Ser Ile Asp Ser Asn Asp Ala Asn Thr Ala Pro Leu His  
 1 5 10 15  
 Lys Lys Thr Ile Ser Ser Leu Ser Gly Ala Val Glu Ser Met Met Lys  
 20 25 30  
 Lys Leu Glu Asp Val Gly Val Leu Val Ala Arg Ile Leu Met Pro Ile  
 35 40 45  
 Leu Phe Ile Thr Ala Gly Trp Gly Lys Ile Thr Gly Tyr Ala Gly Thr  
 50 55 60  
 Gln Gln Tyr Met Glu Ala Met Gly Val Pro Gly Phe Met Leu Pro Leu  
 65 70 75 80  
 Val Ile Leu Leu Glu Phe Gly Gly Gly Leu Ala Ile Leu Phe Gly Phe  
 85 90 95  
 Leu Thr Arg Thr Thr Ala Leu Phe Thr Ala Gly Phe Thr Leu Leu Thr  
 100 105 110  
 Ala Phe Leu Phe His Ser Asn Phe Ala Glu Gly Val Asn Ser Leu Met  
 115 120 125  
 Phe Met Lys Asn Leu Thr Ile Ser Gly Gly Phe Leu Leu Leu Ala Ile  
 130 135 140  
 Thr Gly Pro Gly Ala Tyr Ser Ile Asp Arg Leu Leu Asn Lys Lys Trp  
 145 150 155 160

<210> 337  
 <211> 296  
 <212> PRT  
 <213> E. Coli

<400> 337  
 Met Ile Lys Lys Thr Thr Glu Ile Asp Ala Ile Leu Leu Asn Leu Asn  
 1 5 10 15  
 Lys Ala Ile Asp Ala His Tyr Gln Trp Leu Val Ser Met Phe His Ser  
 20 25 30  
 Val Val Ala Arg Asp Ala Ser Lys Pro Glu Ile Thr Asp Asn His Ser  
 35 40 45  
 Tyr Gly Leu Cys Gln Phe Gly Arg Trp Ile Asp His Leu Gly Pro Leu  
 50 55 60  
 Asp Asn Asp Glu Leu Pro Tyr Val Arg Leu Met Asp Ser Ala His Gln  
 65 70 75 80  
 His Met His Asn Cys Gly Arg Glu Leu Met Leu Ala Ile Val Glu Asn  
 85 90 95  
 His Trp Gln Asp Ala His Phe Asp Ala Phe Gln Glu Gly Leu Leu Ser  
 100 105 110  
 Phe Thr Ala Ala Leu Thr Asp Tyr Lys Ile Tyr Leu Leu Thr Ile Arg  
 115 120 125  
 Ser Asn Met Asp Val Leu Thr Gly Leu Pro Gly Arg Arg Val Leu Asp  
 130 135 140  
 Glu Ser Phe Asp His Gln Leu Arg Asn Ala Glu Pro Leu Asn Leu Tyr  
 145 150 155 160  
 Leu Met Leu Leu Asp Ile Asp Arg Phe Lys Leu Val Asn Asp Thr Tyr  
 165 170 175

Gly His Leu Ile Gly Asp Val Val Leu Arg Thr Leu Ala Thr Tyr Leu  
 180 185 190  
 Ala Ser Trp Thr Arg Asp Tyr Glu Thr Val Tyr Arg Tyr Gly Gly Glu  
 195 200 205  
 Glu Phe Ile Ile Ile Val Lys Ala Ala Asn Asp Glu Glu Ala Cys Arg  
 210 215 220  
 Ala Gly Val Arg Ile Cys Gln Leu Val Asp Asn His Ala Ile Thr His  
 225 230 235 240  
 Ser Glu Gly His Ile Asn Ile Thr Val Thr Ala Gly Val Ser Arg Ala  
 245 250 255  
 Phe Pro Glu Glu Pro Leu Asp Val Val Ile Gly Arg Ala Asp Arg Ala  
 260 265 270  
 Met Tyr Glu Gly Lys Gln Thr Gly Arg Asn Arg Cys Met Phe Ile Asp  
 275 280 285  
 Glu Gln Asn Val Ile Asn Arg Val  
 290 295

<210> 338  
 <211> 203  
 <212> PRT  
 <213> E. Coli

<400> 338  
 Met Arg Leu Arg Val Val Pro Gly Phe Ile Ser Pro Pro Pro Gly Phe  
 1 5 10 15  
 Gly Gly Leu Gly Tyr Thr Pro Thr Ala Arg Ala Cys Val Asn Ile Ser  
 20 25 30  
 Ile Pro Leu Gln Leu Arg Val Ile Asp Met Leu Asp Val Phe Thr Pro  
 35 40 45  
 Leu Leu Lys Leu Phe Ala Asn Glu Pro Leu Glu Arg Leu Met Tyr Thr  
 50 55 60  
 Ile Ile Ile Phe Gly Leu Thr Leu Trp Leu Ile Pro Lys Glu Phe Thr  
 65 70 75 80  
 Val Ala Phe Asn Ala Tyr Thr Glu Ile Pro Trp Leu Phe Gln Ile Ile  
 85 90 95  
 Val Phe Ala Phe Ser Phe Val Val Ala Ile Ser Phe Ser Arg Leu Arg  
 100 105 110  
 Ala His Ile Gln Lys His Tyr Ser Leu Leu Pro Glu Gln Arg Val Leu  
 115 120 125  
 Leu Arg Leu Ser Glu Lys Glu Ile Ala Val Phe Lys Asp Phe Leu Lys  
 130 135 140  
 Thr Gly Asn Leu Ile Ile Thr Ser Pro Cys Arg Asn Pro Val Met Lys  
 145 150 155 160  
 Lys Leu Glu Arg Lys Gly Ile Ile Gln His Gln Ser Asp Ser Ala Asn  
 165 170 175  
 Cys Ser Tyr Tyr Leu Val Thr Glu Lys Tyr Ser His Phe Met Lys Leu  
 180 185 190  
 Phe Trp Asn Ser Arg Ser Arg Arg Phe Asn Arg  
 195 200

<210> 339  
 <211> 58  
 <212> PRT  
 <213> E. Coli

<400> 339  
 Met Leu Leu Gln Pro Ser Ala Arg Thr Ser Phe Gly Phe Lys Cys Phe

1 5 10 15  
 Ala Phe Gly Ile Arg His Gly Ser Glu Arg Ser Ile Leu Val Gly Glu  
 20 25 30  
 His Ala Ala His Gln Gly Phe Val Val Ala Glu Val Asp Phe Leu His  
 35 40 45  
 Phe Ala Asn Leu Thr Ser Cys Cys Tyr Val  
 50 55

<210> 340  
 <211> 1426  
 <212> PRT  
 <213> E. Coli

<400> 340  
 Met Ser Gly Lys Pro Ala Ala Arg Gln Gly Asp Met Thr Gln Tyr Gly  
 1 5 10 15  
 Gly Pro Ile Val Gln Gly Ser Ala Gly Val Arg Ile Gly Ala Pro Thr  
 20 25 30  
 Gly Val Ala Cys Ser Val Cys Pro Gly Gly Met Thr Ser Gly Asn Pro  
 35 40 45  
 Val Asn Pro Leu Leu Gly Ala Lys Val Leu Pro Gly Glu Thr Asp Leu  
 50 55 60  
 Ala Leu Pro Gly Pro Leu Pro Phe Ile Leu Ser Arg Thr Tyr Ser Ser  
 65 70 75 80  
 Tyr Arg Thr Lys Thr Pro Ala Pro Val Gly Val Phe Gly Pro Gly Trp  
 85 90 95  
 Lys Ala Pro Ser Asp Ile Arg Leu Gln Leu Arg Asp Asp Gly Leu Ile  
 100 105 110  
 Leu Asn Asp Asn Gly Gly Arg Ser Ile His Phe Glu Pro Leu Leu Pro  
 115 120 125  
 Gly Glu Ala Val Tyr Ser Arg Ser Glu Ser Met Trp Leu Val Arg Gly  
 130 135 140  
 Gly Lys Ala Ala Gln Pro Asp Gly His Thr Leu Ala Arg Leu Trp Gly  
 145 150 155 160  
 Ala Leu Pro Pro Asp Ile Arg Leu Ser Pro His Leu Tyr Leu Ala Thr  
 165 170 175  
 Asn Ser Ala Gln Gly Pro Trp Trp Ile Leu Gly Trp Ser Glu Arg Val  
 180 185 190  
 Pro Gly Ala Glu Asp Val Leu Pro Ala Pro Leu Pro Pro Tyr Arg Val  
 195 200 205  
 Leu Thr Gly Met Ala Asp Arg Phe Gly Arg Thr Leu Thr Tyr Arg Arg  
 210 215 220  
 Glu Ala Ala Gly Asp Leu Ala Gly Glu Ile Thr Gly Val Thr Asp Gly  
 225 230 235 240  
 Ala Gly Arg Glu Phe Arg Leu Val Leu Thr Thr Gln Ala Gln Arg Ala  
 245 250 255  
 Glu Glu Ala Arg Thr Ser Ser Leu Ser Ser Ser Asp Ser Ser Arg Pro  
 260 265 270  
 Leu Ser Ala Ser Ala Phe Pro Asp Thr Leu Pro Gly Thr Glu Tyr Gly  
 275 280 285  
 Pro Asp Arg Gly Ile Arg Leu Ser Ala Val Trp Leu Met His Asp Pro  
 290 295 300  
 Ala Tyr Pro Glu Ser Leu Pro Ala Ala Pro Leu Val Arg Tyr Thr Tyr  
 305 310 315 320  
 Thr Glu Ala Gly Glu Leu Leu Ala Val Tyr Asp Arg Ser Asn Thr Gln  
 325 330 335  
 Val Arg Ala Phe Thr Tyr Asp Ala Gln His Pro Gly Arg Met Val Ala  
 340 345 350  
 His Arg Tyr Ala Gly Arg Pro Glu Met Arg Tyr Arg Tyr Asp Asp Thr  
 355 360 365

Gly Arg Val Val Glu Gln Leu Asn Pro Ala Gly Leu Ser Tyr Arg Tyr  
 370 375 380  
 Leu Tyr Glu Gln Asp Arg Ile Thr Val Thr Asp Ser Leu Asn Arg Arg  
 385 390 395 400  
 Glu Val Leu His Thr Glu Gly Gly Ala Gly Leu Lys Arg Val Val Lys  
 405 410 415  
 Lys Glu Leu Ala Asp Gly Ser Val Thr Arg Ser Gly Tyr Asp Ala Ala  
 420 425 430  
 Gly Arg Leu Thr Ala Gln Thr Asp Ala Ala Gly Arg Arg Thr Glu Tyr  
 435 440 445  
 Gly Leu Asn Val Val Ser Gly Asp Ile Thr Asp Ile Thr Thr Pro Asp  
 450 455 460  
 Gly Arg Glu Thr Lys Phe Tyr Tyr Asn Asp Gly Asn Gln Leu Thr Ala  
 465 470 475 480  
 Val Val Ser Pro Asp Gly Leu Glu Ser Arg Arg Glu Tyr Asp Glu Pro  
 485 490 495  
 Gly Arg Leu Val Ser Glu Thr Ser Arg Ser Gly Glu Thr Val Arg Tyr  
 500 505 510  
 Arg Tyr Asp Asp Ala His Ser Glu Leu Pro Ala Thr Thr Thr Asp Ala  
 515 520 525  
 Thr Gly Ser Thr Arg Gln Met Thr Trp Ser Arg Tyr Gly Gln Leu Leu  
 530 535 540  
 Ala Phe Thr Asp Cys Ser Gly Tyr Gln Thr Arg Tyr Glu Tyr Asp Arg  
 545 550 555 560  
 Phe Gly Gln Met Thr Ala Val His Arg Glu Glu Gly Ile Ser Leu Tyr  
 565 570 575  
 Arg Arg Tyr Asp Asn Arg Gly Arg Leu Thr Ser Val Lys Asp Ala Gln  
 580 585 590  
 Gly Arg Glu Thr Arg Tyr Glu Tyr Asn Ala Ala Gly Asp Leu Thr Ala  
 595 600 605  
 Val Ile Thr Pro Asp Gly Asn Arg Ser Glu Thr Gln Tyr Asp Ala Trp  
 610 615 620  
 Gly Lys Ala Val Ser Thr Thr Gln Gly Gly Leu Thr Arg Ser Met Glu  
 625 630 635 640  
 Tyr Asp Ala Ala Gly Arg Val Ile Ser Leu Thr Asn Glu Asn Gly Ser  
 645 650 655  
 His Ser Val Phe Ser Tyr Asp Ala Leu Asp Arg Leu Val Gln Gln Gly  
 660 665 670  
 Gly Phe Asp Gly Arg Thr Gln Arg Tyr His Tyr Asp Leu Thr Gly Lys  
 675 680 685  
 Leu Thr Gln Ser Glu Asp Glu Gly Leu Val Ile Leu Trp Tyr Tyr Asp  
 690 695 700  
 Glu Ser Asp Arg Ile Thr His Arg Thr Val Asn Gly Glu Pro Ala Glu  
 705 710 715 720  
 Gln Trp Gln Tyr Asp Gly His Gly Trp Leu Thr Asp Ile Ser His Leu  
 725 730 735  
 Ser Glu Gly His Arg Val Ala Val His Tyr Gly Tyr Asp Asp Lys Gly  
 740 745 750  
 Arg Leu Thr Gly Glu Cys Gln Thr Val Glu Asn Pro Glu Thr Gly Glu  
 755 760 765  
 Leu Leu Trp Gln His Glu Thr Lys His Ala Tyr Asn Glu Gln Gly Leu  
 770 775 780  
 Ala Asn Arg Val Thr Pro Asp Ser Leu Pro Pro Val Glu Trp Leu Thr  
 785 790 795 800  
 Tyr Gly Ser Gly Tyr Leu Ala Gly Met Lys Leu Gly Gly Thr Pro Leu  
 805 810 815  
 Val Glu Tyr Thr Arg Asp Arg Leu His Arg Glu Thr Val Arg Ser Phe  
 820 825 830  
 Gly Ser Met Ala Gly Ser Asn Ala Ala Tyr Glu Leu Thr Ser Thr Tyr  
 835 840 845  
 Thr Pro Ala Gly Gln Leu Gln Ser Gln His Leu Asn Ser Leu Val Tyr

850	855	860
Asp Arg Asp Tyr Gly Trp Ser Asp Asn Gly Asp Leu Val Arg Ile Ser		
865	870	875
Gly Pro Arg Gln Thr Arg Glu Tyr Gly Tyr Ser Ala Thr Gly Arg Leu		880
	885	890
Glu Ser Val Arg Thr Leu Ala Pro Asp Leu Asp Ile Arg Ile Pro Tyr		895
	900	905
Ala Thr Asp Pro Ala Gly Asn Arg Leu Pro Asp Pro Glu Leu His Pro		910
	915	920
Asp Ser Thr Leu Thr Val Trp Pro Asp Asn Arg Ile Ala Glu Asp Ala		925
	930	935
His Tyr Val Tyr Arg His Asp Glu Tyr Gly Arg Leu Thr Glu Lys Thr		940
	945	950
Asp Arg Ile Pro Ala Gly Val Ile Arg Thr Asp Asp Glu Arg Thr His		955
	965	970
His Tyr His Tyr Asp Ser Gln His Arg Leu Val Phe Tyr Thr Arg Ile		975
	980	985
Gln His Gly Glu Pro Leu Val Glu Ser Arg Tyr Leu Tyr Asp Pro Leu		990
	995	1000
Gly Arg Arg Met Ala Lys Arg Val Trp Arg Arg Glu Arg Asp Leu Thr		1005
	1010	1015
Gly Trp Met Ser Leu Ser Arg Lys Pro Glu Val Thr Trp Tyr Gly Trp		1020
	1025	1030
Asp Gly Asp Arg Leu Thr Thr Val Gln Thr Asp Thr Thr Arg Ile Gln		1035
	1045	1050
Thr Val Tyr Glu Pro Gly Ser Phe Thr Pro Leu Ile Arg Val Glu Thr		1055
	1060	1065
Glu Asn Gly Glu Arg Glu Lys Ala Gln Arg Arg Ser Leu Ala Glu Thr		1070
	1075	1080
Leu Gln Gln Glu Gly Ser Glu Asn Gly His Gly Val Val Phe Pro Ala		1085
	1090	1095
Glu Leu Val Arg Leu Leu Asp Arg Leu Glu Glu Ile Arg Ala Asp		1100
	1105	1110
Arg Val Ser Ser Glu Ser Arg Ala Trp Leu Ala Gln Cys Gly Leu Thr		1115
	1125	1130
Val Glu Gln Leu Ala Arg Gln Val Glu Pro Glu Tyr Thr Pro Ala Arg		1135
	1140	1145
Lys Ala His Leu Tyr His Cys Asp His Arg Gly Leu Pro Leu Ala Leu		1150
	1155	1160
Ile Ser Glu Asp Gly Asn Thr Ala Trp Ser Ala Glu Tyr Asp Glu Trp		1165
	1170	1175
Gly Asn Gln Leu Asn Glu Glu Asn Pro His His Val Tyr Gln Pro Tyr		1180
	1185	1190
Arg Leu Pro Gly Gln Gln His Asp Glu Glu Ser Gly Leu Tyr Tyr Asn		1195
	1205	1210
Arg His Arg Tyr Tyr Asp Pro Leu Gln Gly Arg Tyr Ile Thr Gln Asp		1215
	1220	1225
Pro Met Gly Leu Lys Gly Gly Trp Asn Leu Tyr Gln Tyr Pro Leu Asn		1230
	1235	1240
Pro Leu Gln Gln Ile Asp Pro Met Gly Leu Leu Gln Thr Trp Asp Asp		1245
	1250	1255
Ala Arg Ser Gly Ala Cys Thr Gly Gly Val Cys Gly Val Leu Ser Arg		1260
	1265	1270
Ile Ile Gly Pro Ser Lys Phe Asp Ser Thr Ala Asp Ala Ala Leu Asp		1275
	1285	1290
Ala Leu Lys Glu Thr Gln Asn Arg Ser Leu Cys Asn Asp Met Glu Tyr		1295
	1300	1305
Ser Gly Ile Val Cys Lys Asp Thr Asn Gly Lys Tyr Phe Ala Ser Lys		1310
	1315	1320
Ala Glu Thr Asp Asn Leu Arg Lys Glu Ser Tyr Pro Leu Lys Arg Lys		1325
	1330	1335
		1340

Cys Pro Thr Gly Thr Asp Arg Val Ala Ala Tyr His Thr His Gly Ala  
 1345 1350 1355 1360  
 Asp Ser His Gly Asp Tyr Val Asp Glu Phe Phe Ser Ser Ser Asp Lys  
 1365 1370 1375  
 Asn Leu Val Arg Ser Lys Asp Asn Asn Leu Glu Ala Phe Tyr Leu Ala  
 1380 1385 1390  
 Thr Pro Asp Gly Arg Phe Glu Ala Leu Asn Asn Lys Gly Glu Tyr Ile  
 1395 1400 1405  
 Phe Ile Arg Asn Ser Val Pro Gly Leu Ser Ser Val Cys Ile Pro Tyr  
 1410 1415 1420  
 His Asp  
 1425

<210> 341  
 <211> 122  
 <212> PRT  
 <213> E. Coli

<400> 341  
 Met Lys Tyr Ser Ser Ile Phe Ser Met Leu Ser Phe Phe Ile Leu Phe  
 1 5 10 15  
 Ala Cys Asn Glu Thr Ala Val Tyr Gly Ser Asp Glu Asn Ile Ile Phe  
 20 25 30  
 Met Arg Tyr Val Glu Lys Leu His Leu Asp Lys Tyr Ser Val Lys Asn  
 35 40 45  
 Thr Val Lys Thr Glu Thr Met Ala Ile Gln Leu Ala Glu Ile Tyr Val  
 50 55 60  
 Arg Tyr Arg Tyr Gly Glu Arg Ile Ala Glu Glu Lys Pro Tyr Leu  
 65 70 75 80  
 Ile Thr Glu Leu Pro Asp Ser Trp Val Val Glu Gly Ala Lys Leu Pro  
 85 90 95  
 Tyr Glu Val Ala Gly Gly Val Phe Ile Ile Glu Ile Asn Lys Lys Asn  
 100 105 110  
 Gly Cys Val Leu Asn Phe Leu His Ser Lys  
 115 120

<210> 342  
 <211> 236  
 <212> PRT  
 <213> E. Coli

<400> 342  
 Met Leu Ala Leu Met Asp Ala Asp Gly Asn Ile Ala Trp Ser Gly Glu  
 1 5 10 15  
 Tyr Asp Glu Trp Gly Asn Gln Leu Asn Glu Glu Asn Pro His His Leu  
 20 25 30  
 His Gln Pro Tyr Arg Leu Pro Gly Gln Gln Tyr Asp Lys Glu Ser Gly  
 35 40 45  
 Leu Tyr Tyr Asn Arg Asn Arg Tyr Tyr Asp Pro Leu Gln Gly Arg Tyr  
 50 55 60  
 Ile Thr Gln Asp Pro Ile Gly Leu Glu Gly Gly Trp Ser Leu Tyr Ala  
 65 70 75 80  
 Tyr Pro Leu Asn Pro Val Asn Gly Ile Asp Pro Leu Gly Leu Ser Pro  
 85 90 95  
 Ala Asp Val Ala Leu Ile Arg Arg Lys Asp Gln Leu Asn His Gln Arg  
 100 105 110  
 Ala Trp Asp Ile Leu Ser Asp Thr Tyr Glu Asp Met Lys Arg Leu Asn  
 115 120 125  
 Leu Gly Gly Thr Asp Gln Phe Phe His Cys Met Ala Phe Cys Arg Val

130 135 140  
 Ser Lys Leu Asn Asp Ala Gly Val Ser Arg Ser Ala Lys Gly Leu Gly  
 145 150 155 160  
 Tyr Glu Lys Glu Ile Arg Asp Tyr Gly Leu Asn Leu Phe Gly Met Tyr  
 165 170 175  
 Gly Arg Lys Val Lys Leu Ser His Ser Glu Met Ile Glu Asp Asn Lys  
 180 185 190  
 Lys Asp Leu Ala Val Asn Asp His Gly Leu Thr Cys Pro Ser Thr Thr  
 195 200 205  
 Asp Cys Ser Asp Arg Cys Ser Asp Tyr Ile Asn Pro Glu His Lys Lys  
 210 215 220  
 Thr Ile Lys Ala Leu Gln Asp Ala Gly Tyr Leu Lys  
 225 230 235

<210> 343  
 <211> 86  
 <212> PRT  
 <213> E. Coli

<400> 343  
 Met Leu Ala Ile Ser Ser Asn Leu Ser Lys Met Ile Ile Phe Ile Phe  
 1 5 10 15  
 Ala Ile Ile Ile Ile Val Val Leu Cys Val Ile Thr Tyr Leu Tyr Leu  
 20 25 30  
 Tyr Lys Asp Glu Ser Leu Val Ser Lys His Tyr Ile Asn Tyr Met Ala  
 35 40 45  
 Ile Pro Glu Asn Asp Gly Val Phe Thr Trp Leu Pro Asp Phe Phe Pro  
 50 55 60  
 His Val Ala Val Asp Ile Ser Ile Tyr Thr Asn Val Glu Asp Asp Tyr  
 65 70 75 80  
 Phe Phe Leu Ile Phe Pro  
 85

<210> 344  
 <211> 63  
 <212> PRT  
 <213> E. Coli

<400> 344  
 Met Arg Ala Arg Glu Gln Val Ala Lys Ile Val Ser Lys Asn Asp Pro  
 1 5 10 15  
 Asp Thr Lys Lys Val Trp Cys Lys Tyr Gly Lys Ile Pro Gly Gln Gly  
 20 25 30  
 Asp Gly Val Asn Leu Phe Phe Val Gly Glu Ile Asn Val Thr His Tyr  
 35 40 45  
 Phe Ile Thr Asn Ile Gly Ala Gly Leu Pro Asp Ala Cys Ala Glu  
 50 55 60

<210> 345  
 <211> 167  
 <212> PRT  
 <213> E. Coli

<400> 345  
 Met Pro Gly Asn Ser Pro His Tyr Gly Arg Trp Pro Gln His Asp Phe  
 1 5 10 15

Thr Ser Leu Lys Lys Leu Arg Pro Gln Ser Val Thr Ser Arg Ile Gln  
 20 25 30  
 Pro Gly Ser Asp Val Ile Val Cys Ala Glu Met Asp Glu Gln Trp Gly  
 35 40 45  
 Tyr Val Gly Ala Lys Ser Arg Gln Arg Trp Leu Phe Tyr Ala Tyr Asp  
 50 55 60  
 Ser Leu Arg Lys Thr Val Val Ala His Val Phe Gly Glu Arg Thr Met  
 65 70 75 80  
 Ala Thr Leu Gly Arg Leu Met Ser Leu Leu Ser Pro Phe Asp Val Val  
 85 90 95  
 Ile Trp Met Thr Asp Gly Trp Pro Leu Tyr Glu Ser Arg Leu Lys Gly  
 100 105 110  
 Lys Leu His Val Ile Ser Lys Arg Tyr Thr Gln Arg Ile Glu Arg His  
 115 120 125  
 Asn Leu Asn Leu Arg Gln His Leu Ala Arg Leu Gly Arg Lys Ser Leu  
 130 135 140  
 Ser Phe Ser Lys Ser Val Glu Leu His Asp Lys Val Ile Gly His Tyr  
 145 150 155 160  
 Leu Asn Ile Lys His Tyr Gln  
 165

<210> 346  
 <211> 91  
 <212> PRT  
 <213> E. Coli

<400> 346  
 Met Ala Ser Val Ser Ile Ser Cys Pro Ser Cys Ser Ala Thr Asp Gly  
 1 5 10 15  
 Val Val Arg Asn Gly Lys Ser Thr Ala Gly His Gln Arg Tyr Leu Cys  
 20 25 30  
 Ser His Cys Arg Lys Thr Trp Gln Leu Gln Phe Thr Tyr Thr Ala Ser  
 35 40 45  
 Gln Pro Gly Thr His Gln Lys Ile Ile Asp Met Ala Met Asn Gly Val  
 50 55 60  
 Gly Cys Arg Ala Thr Ala Arg Ile Met Gly Val Gly Leu Asn Thr Ile  
 65 70 75 80  
 Leu Arg His Leu Lys Asn Ser Gly Arg Ser Arg  
 85 90

<210> 347  
 <211> 138  
 <212> PRT  
 <213> E. Coli

<400> 347  
 Met Met Thr Lys Thr Gln Ile Asn Lys Leu Ile Lys Met Met Asn Asp  
 1 5 10 15  
 Leu Asp Tyr Pro Phe Glu Ala Pro Leu Lys Glu Ser Phe Ile Glu Ser  
 20 25 30  
 Ile Ile Gln Ile Glu Phe Asn Ser Asn Ser Thr Asn Cys Leu Glu Lys  
 35 40 45  
 Leu Cys Asn Glu Val Ser Ile Leu Phe Lys Asn Gln Pro Asp Tyr Leu  
 50 55 60  
 Thr Phe Leu Arg Ala Met Asp Gly Phe Glu Val Asn Gly Leu Arg Leu  
 65 70 75 80  
 Phe Ser Leu Ser Ile Pro Glu Pro Ser Val Lys Asn Leu Phe Ala Val  
 85 90 95



Asn Glu Phe Tyr Arg Asn Asn Asp Asp Phe Ile Asn Pro Asp Leu Gln  
 100 105 110  
 Glu Arg Leu Val Ile Gly Asp Tyr Ser Ile Ser Ile Phe Thr Tyr Asp  
 115 120 125  
 Ile Lys Gly Asp Ala Ala Asn Leu Leu Ile  
 130 135

&lt;210&gt; 348

&lt;211&gt; 392

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 348

Met Ser Asn Ile Val Tyr Leu Thr Val Thr Gly Glu Gln Gln Gly Ser  
 1 5 10 15  
 Ile Ser Ala Gly Cys Gly Thr Ser Glu Ser Thr Gly Asn Arg Trp Gln  
 20 25 30  
 Ser Gly His Glu Asp Glu Ile Phe Thr Phe Ser Leu Leu Asn Asn Ile  
 35 40 45  
 Asn Asn Thr Gly Leu Gly Ser Gln Phe His Gly Ile Thr Phe Cys Lys  
 50 55 60  
 Leu Ile Asp Lys Ser Thr Pro Leu Phe Ile Asn Ser Ile Asn Asn Asn  
 65 70 75 80  
 Glu Gln Leu Phe Met Gly Phe Asp Phe Tyr Arg Ile Asn Arg Phe Gly  
 85 90 95  
 Arg Leu Glu Lys Tyr Tyr Tyr Ile Gln Leu Arg Gly Ala Phe Leu Ser  
 100 105 110  
 Ala Ile His His Gln Ile Ile Glu Asn Gln Leu Asp Thr Glu Thr Ile  
 115 120 125  
 Thr Ile Ser Tyr Glu Phe Ile Leu Cys Gln His Leu Ile Ala Asn Thr  
 130 135 140  
 Glu Phe Ser Tyr Leu Ala Leu Pro Glu Asn Tyr Asn Arg Leu Phe Leu  
 145 150 155 160  
 Pro Asn Ser Lys Asn Gln Thr Asn Asn Arg Phe Lys Thr Leu Asn Ser  
 165 170 175  
 Lys Ala Ile Gly Arg Leu Leu Ala Ala Gly Gly Val Tyr Asn Gly Asn  
 180 185 190  
 Ile Glu Gly Phe Arg Asp Thr Ala Glu Lys Leu Gly Gly Asp Ala Ile  
 195 200 205  
 Lys Gly Tyr Asp Gln Ile Leu Asn Glu Lys Thr Ala Gly Ile Ala Ile  
 210 215 220  
 Ala Thr Ala Ser Ile Leu Leu Thr Lys Arg Ser Asn Val Asp Thr Tyr  
 225 230 235 240  
 Thr Glu Ile Asn Ser Tyr Leu Gly Lys Leu Arg Gly Gln Gln Lys Leu  
 245 250 255  
 Leu Asp Gly Ile Asp Ile Ile Glu Ile Ile Tyr Ile Lys Arg Pro Ser  
 260 265 270  
 Lys Asp Leu Ala Asn Leu Arg Lys Glu Phe Asn Lys Thr Val Arg Lys  
 275 280 285  
 Asn Phe Leu Ile Lys Leu Ala Lys Thr Ser Glu Ala Ser Gly Arg Phe  
 290 295 300  
 Asn Ala Glu Asp Leu Leu Arg Met Arg Lys Gly Asn Val Pro Leu Asn  
 305 310 315 320  
 Tyr Asn Val His His Lys Leu Ser Leu Asp Asp Gly Gly Thr Asn Asp  
 325 330 335  
 Phe Glu Asn Leu Val Leu Ile Glu Asn Glu Pro Tyr His Lys Val Phe  
 340 345 350  
 Thr Asn Met Gln Ser Arg Ile Ala Lys Gly Ile Leu Val Gly Glu Ser  
 355 360 365  
 Lys Ile Thr Pro Trp Ala Ile Pro Ser Gly Ser Ile Tyr Pro Pro Met

370  
Lys Asn Ile Met Asp His Thr Lys  
385 390

380

<210> 349  
<211> 221  
<212> PRT  
<213> E. Coli

<400> 349  
Met Val Leu Ala Leu Asn Tyr Asn Met His Gly Val Asn Ile Arg Ser  
1 5 10 15  
Glu Asn Ala Ala Lys Pro His Thr Met Pro Ser Arg Tyr Leu Cys Glu  
20 25 30  
Tyr Ile Arg Ser Ile Glu Lys Asn Gly His Ala Leu Asp Phe Gly Cys  
35 40 45  
Gly Lys Leu Arg Tyr Ser Asp Glu Leu Ile Ser Lys Phe Asp Glu Val  
50 55 60  
Thr Phe Leu Asp Ser Lys Arg Gln Leu Glu Arg Glu Gln Ile Ile Arg  
65 70 75 80  
Gly Ile Lys Thr Lys Ile Ile Asp Tyr Val Pro Arg Tyr Tyr Lys Asn  
85 90 95  
Ala Asn Thr Val Ala Phe Glu Asp Val Asp Lys Ile Ile Gly Gly Tyr  
100 105 110  
Asp Phe Ile Leu Cys Ser Asn Val Leu Ser Ala Val Pro Cys Arg Asp  
115 120 125  
Thr Ile Asp Lys Ile Val Leu Ser Ile Lys Arg Leu Leu Lys Ser Gly  
130 135 140  
Gly Glu Thr Leu Ile Val Asn Gln Tyr Lys Ser Ser Tyr Phe Lys Lys  
145 150 155 160  
Tyr Glu Thr Gly Arg Lys His Leu Tyr Gly Tyr Ile Tyr Lys Asn Ser  
165 170 175  
Lys Ser Val Ser Tyr Tyr Gly Leu Leu Asp Glu Leu Ala Val Gln Glu  
180 185 190  
Ile Cys Ser Ser His Gly Leu Glu Ile Leu Lys Ser Trp Ser Lys Ala  
195 200 205  
Gly Ser Ser Tyr Val Thr Val Gly Ser Cys Asn Ala Ile  
210 215 220

<210> 350  
<211> 234  
<212> PRT  
<213> E. Coli

<400> 350  
Met Asn Asn Met Phe Glu Pro Pro Lys Asn Tyr Asn Glu Met Leu Pro  
1 5 10 15  
Lys Leu His Lys Ala Thr Phe Leu Asn Thr Leu Ile Tyr Cys Ile Leu  
20 25 30  
Leu Val Ile Tyr Glu Tyr Ile Pro Leu Ile Thr Leu Pro Thr Lys Tyr  
35 40 45  
Val Pro Pro Ile Lys Asp His Glu Ser Phe Ile Asn Trp Ala Leu Ser  
50 55 60  
Phe Gly Ile Leu Pro Cys Ala Phe Ala Ile Phe Ala Tyr Leu Ile Ser  
65 70 75 80  
Gly Ala Leu Asp Leu His Asn Asn Ala Ala Lys Leu Leu Arg Val Arg  
85 90 95  
Tyr Leu Trp Asp Lys His Leu Ile Ile Lys Pro Leu Ser Arg Arg Ala

100	105	110
Gly Val Asn Arg Lys Leu Asn Lys Asp Glu Ala His Asn Val Met Ser		
115	120	125
Asn Leu Tyr Tyr Pro Glu Val Arg Lys Ile Glu Asp Lys His Tyr Ile		
130	135	140
Glu Leu Phe Trp Asn Lys Val Tyr Tyr Phe Trp Ile Phe Phe Glu Phe		
145	150	155
Ser Ile Ile Ala Leu Ile Ser Phe Leu Ile Ile Phe Phe Cys Lys Gln		
165	170	175
Met Asp Ile Phe His Val Glu Gly Ser Leu Leu Ser Leu Phe Phe		
180	185	190
Val Ile Leu Ser Phe Ser Val Ser Gly Ile Ile Phe Ala Leu Thr Val		
195	200	205
Lys Pro Arg Thr Glu Ser Gln Val Gly Lys Ile Pro Asp Asp Lys Ile		
210	215	220
Lys Glu Phe Phe Thr Lys Asn Asn Ile Asn		
225	230	

<210> 351  
 <211> 94  
 <212> PRT  
 <213> E. Coli

<400> 351
Met Phe Thr Ile Asn Ala Glu Val Arg Lys Glu Gln Gly Lys Gly Ala
1 5 10 15
Ser Arg Arg Leu Arg Ala Ala Asn Lys Phe Pro Ala Ile Ile Tyr Gly
20 25 30
Gly Lys Glu Ala Pro Leu Ala Ile Glu Leu Asp His Asp Lys Val Met
35 40 45
Asn Met Gln Ala Lys Ala Glu Phe Tyr Ser Glu Val Leu Thr Ile Val
50 55 60
Val Asp Gly Lys Glu Ile Lys Val Lys Ala Gln Asp Val Gln Arg His
65 70 75 80
Pro Tyr Lys Pro Lys Leu Gln His Ile Asp Phe Val Arg Ala
85 90

<210> 352  
 <211> 658  
 <212> PRT  
 <213> E. Coli

<400> 352
Met Val Leu Phe Tyr Arg Ala His Trp Arg Asp Tyr Lys Asn Asp Gln
1 5 10 15
Val Arg Ile Met Met Asn Leu Thr Thr Leu Thr His Arg Asp Ala Leu
20 25 30
Cys Leu Asn Ala Arg Phe Thr Ser Arg Glu Glu Ala Ile His Ala Leu
35 40 45
Thr Gln Arg Leu Ala Ala Leu Gly Lys Ile Ser Ser Thr Glu Gln Phe
50 55 60
Leu Glu Glu Val Tyr Arg Arg Glu Ser Leu Gly Pro Thr Ala Leu Gly
65 70 75 80
Glu Gly Leu Ala Val Pro His Gly Lys Thr Ala Ala Val Lys Glu Ala
85 90 95
Ala Phe Ala Val Ala Thr Leu Ser Glu Pro Leu Gln Trp Glu Gly Val
100 105 110
Asp Gly Pro Glu Ala Val Asp Leu Val Val Leu Leu Ala Ile Pro Pro

115	120	125
Asn Glu Ala Gly Thr Thr His Met Gln Leu Leu Thr Ala Leu Thr Thr		
130	135	140
Arg Leu Ala Asp Asp Glu Ile Arg Ala Arg Ile Gln Ser Ala Thr Thr		
145	150	155
Pro Asp Glu Leu Leu Ser Ala Leu Asp Asp Lys Gly Gly Thr Gln Pro		
165	170	175
Ser Ala Ser Phe Ser Asn Ala Pro Thr Ile Val Cys Val Thr Ala Cys		
180	185	190
Pro Ala Gly Ile Ala His Thr Tyr Met Ala Ala Glu Tyr Leu Glu Lys		
195	200	205
Ala Gly Arg Lys Leu Gly Val Asn Val Tyr Val Glu Lys Gln Gly Ala		
210	215	220
Asn Gly Ile Glu Gly Arg Leu Thr Ala Asp Gln Leu Asn Ser Ala Thr		
225	230	235
Ala Cys Ile Phe Ala Ala Glu Val Ala Ile Lys Glu Ser Glu Arg Phe		
245	250	255
Asn Gly Ile Pro Ala Leu Ser Val Pro Val Ala Glu Pro Ile Arg His		
260	265	270
Ala Glu Ala Leu Ile Gln Gln Ala Leu Thr Leu Lys Arg Ser Asp Glu		
275	280	285
Thr Arg Thr Val Gln Gln Asp Thr Gln Pro Val Lys Ser Val Lys Thr		
290	295	300
Glu Leu Lys Gln Ala Leu Leu Ser Gly Ile Ser Phe Ala Val Pro Leu		
305	310	315
Ile Val Ala Gly Gly Thr Val Leu Ala Val Ala Val Leu Leu Ser Gln		
325	330	335
Ile Phe Gly Leu Gln Asp Leu Phe Asn Glu Glu Asn Ser Trp Leu Trp		
340	345	350
Met Tyr Arg Lys Leu Gly Gly Gly Leu Leu Gly Ile Leu Met Val Pro		
355	360	365
Val Leu Ala Ala Tyr Thr Ala Tyr Ser Leu Ala Asp Lys Pro Ala Leu		
370	375	380
Ala Pro Gly Phe Ala Ala Gly Leu Ala Ala Asn Met Ile Gly Ser Gly		
385	390	395
Phe Leu Gly Ala Val Val Gly Gly Leu Ile Ala Gly Tyr Leu Met Arg		
405	410	415
Trp Val Lys Asn His Leu Arg Leu Ser Lys Phe Asn Gly Phe Leu		
420	425	430
Thr Phe Tyr Leu Tyr Pro Val Leu Gly Thr Leu Gly Ala Gly Ser Leu		
435	440	445
Met Leu Phe Val Val Gly Glu Pro Val Ala Trp Ile Asn Asn Ser Leu		
450	455	460
Thr Ala Trp Leu Asn Gly Leu Ser Gly Ser Asn Ala Leu Leu Leu Gly		
465	470	475
Ala Ile Leu Gly Phe Met Cys Ser Phe Asp Leu Gly Gly Pro Val Asn		
485	490	495
Lys Ala Ala Tyr Ala Phe Cys Leu Gly Ala Met Ala Asn Gly Val Tyr		
500	505	510
Gly Pro Tyr Ala Ile Phe Ala Ser Val Lys Met Val Ser Ala Phe Thr		
515	520	525
Val Thr Ala Ser Thr Met Leu Ala Pro Arg Leu Phe Lys Glu Phe Glu		
530	535	540
Ile Glu Thr Gly Lys Ser Thr Trp Leu Leu Gly Leu Ala Gly Ile Thr		
545	550	555
Glu Gly Ala Ile Pro Met Ala Ile Glu Asp Pro Leu Arg Val Ile Gly		
565	570	575
Ser Phe Val Leu Gly Ser Met Val Thr Gly Ala Ile Val Gly Ala Met		
580	585	590
Asn Ile Gly Leu Ser Thr Pro Gly Ala Gly Ile Phe Ser Leu Phe Leu		
595	600	605

Leu His Asp Asn Gly Ala Gly Gly Val Met Ala Ala Ile Gly Trp Phe  
 610 615 620  
 Gly Ala Ala Leu Val Gly Ala Ala Ile Ser Thr Ala Ile Leu Leu Met  
 625 630 635 640  
 Trp Arg Arg His Ala Val Lys His Gly Asn Tyr Leu Thr Asp Gly Val  
 645 650 655  
 Met Pro

<210> 353  
 <211> 877  
 <212> PRT  
 <213> E. Coli

<400> 353  
 Met Lys Ala Val Ser Arg Val His Ile Thr Pro His Met His Trp Asp  
 1 5 10 15  
 Arg Glu Trp Tyr Phe Thr Thr Glu Glu Ser Arg Ile Leu Leu Val Asn  
 20 25 30  
 Asn Met Glu Glu Ile Leu Cys Arg Leu Glu Gln Asp Asn Glu Tyr Lys  
 35 40 45  
 Tyr Tyr Val Leu Asp Gly Gln Thr Ala Ile Leu Glu Asp Tyr Phe Ala  
 50 55 60  
 Val Lys Pro Glu Asn Lys Asp Arg Val Lys Lys Gln Val Glu Ala Gly  
 65 70 75 80  
 Lys Leu Ile Ile Gly Pro Trp Tyr Thr Gln Thr Asp Thr Thr Ile Val  
 85 90 95  
 Ser Ala Glu Ser Ile Val Arg Asn Leu Met Tyr Gly Met Arg Asp Cys  
 100 105 110  
 Leu Ala Phe Gly Glu Pro Met Lys Ile Gly Tyr Leu Pro Asp Ser Phe  
 115 120 125  
 Gly Met Ser Gly Gln Leu Pro His Ile Tyr Asn Gly Phe Gly Ile Thr  
 130 135 140  
 Arg Thr Met Phe Trp Arg Gly Cys Ser Glu Arg His Gly Thr Asp Lys  
 145 150 155 160  
 Thr Glu Phe Leu Trp Gln Ser Ser Asp Gly Ser Glu Val Thr Ala Gln  
 165 170 175  
 Val Leu Pro Leu Gly Tyr Ala Ile Gly Lys Tyr Leu Pro Ala Asp Glu  
 180 185 190  
 Asn Gly Leu Arg Lys Arg Leu Asp Ser Tyr Phe Asp Val Leu Glu Lys  
 195 200 205  
 Ala Ser Val Thr Lys Glu Ile Leu Leu Pro Asn Gly His Asp Gln Met  
 210 215 220  
 Pro Leu Gln Gln Asn Ile Phe Glu Val Met Asp Lys Leu Arg Glu Ile  
 225 230 235 240  
 Tyr Pro Gln Arg Lys Phe Val Met Ser Arg Phe Glu Glu Val Phe Glu  
 245 250 255  
 Lys Ile Glu Ala Gln Arg Asp Asn Leu Ala Thr Leu Lys Gly Glu Phe  
 260 265 270  
 Ile Asp Gly Lys Tyr Met Arg Val His Arg Thr Ile Gly Ser Thr Arg  
 275 280 285  
 Met Asp Ile Lys Ile Ala His Ala Arg Ile Glu Asn Lys Ile Val Asn  
 290 295 300  
 Leu Leu Glu Pro Leu Ala Thr Leu Ala Trp Thr Leu Gly Phe Glu Tyr  
 305 310 315 320  
 His His Gly Leu Leu Glu Lys Met Trp Lys Glu Ile Leu Lys Asn His  
 325 330 335  
 Ala His Asp Ser Ile Gly Cys Cys Cys Ser Asp Lys Val His Arg Glu  
 340 345 350  
 Ile Val Ala Arg Phe Glu Leu Ala Glu Asp Met Ala Asp Asn Leu Ile

355	360	365
Arg Phe Tyr Met Arg Lys Ile Ala Asp Asn Met Pro Gln Ser Asp Ala		
370	375	380
Asp Lys Leu Val Leu Phe Asn Leu Met Pro Trp Pro Arg Glu Glu Val		
385	390	395
Ile Asn Thr Thr Val Arg Leu Arg Ala Ser Gln Phe Asn Leu Arg Asp		
405	410	415
Asp Arg Gly Gln Pro Val Pro Tyr Phe Ile Arg His Ala Arg Glu Ile		
420	425	430
Asp Pro Gly Leu Ile Asp Arg Gln Ile Val His Tyr Gly Asn Tyr Asp		
435	440	445
Pro Phe Met Glu Phe Asp Ile Gln Ile Asn Gln Ile Val Pro Ser Met		
450	455	460
Gly Tyr Arg Thr Leu Tyr Ile Glu Ala Asn Gln Pro Gly Asn Val Ile		
465	470	475
Ala Ala Lys Ser Asp Ala Glu Gly Ile Leu Glu Asn Ala Phe Trp Gln		
485	490	495
Ile Ala Leu Asn Glu Asp Gly Ser Leu Gln Leu Val Asp Lys Asp Ser		
500	505	510
Gly Val Arg Tyr Asp Arg Val Leu Gln Ile Glu Glu Ser Ser Asp Asp		
515	520	525
Gly Asp Glu Tyr Asp Tyr Ser Pro Ala Lys Glu Glu Trp Val Ile Thr		
530	535	540
Ala Ala Asn Ala Lys Pro Gln Cys Asp Ile Ile His Glu Ala Trp Gln		
545	550	555
Ser Arg Ala Val Ile Arg Tyr Asp Met Ala Val Pro Leu Asn Leu Ser		
565	570	575
Glu Arg Ser Ala Arg Gln Ser Thr Gly Arg Val Gly Val Val Leu Val		
580	585	590
Val Thr Leu Ser His Asn Ser Arg Arg Ile Asp Val Asp Ile Asn Leu		
595	600	605
Asp Asn Gln Ala Asp Asp His Arg Leu Arg Val Leu Val Pro Thr Pro		
610	615	620
Phe Asn Thr Asp Ser Val Leu Ala Asp Thr Gln Phe Gly Ser Leu Thr		
625	630	635
Arg Pro Val Asn Asp Ser Ala Met Asn Asn Trp Gln Gln Glu Gly Trp		
645	650	655
Lys Glu Ala Pro Val Pro Val Trp Asn Met Leu Asn Tyr Val Ala Leu		
660	665	670
Gln Glu Gly Arg Asn Gly Met Ala Val Phe Ser Glu Gly Leu Arg Glu		
675	680	685
Phe Glu Val Ile Gly Glu Glu Lys Lys Thr Phe Ala Ile Thr Leu Leu		
690	695	700
Arg Gly Val Gly Leu Leu Gly Lys Glu Asp Leu Leu Leu Arg Pro Gly		
705	710	715
Arg Pro Ser Gly Ile Lys Met Pro Val Pro Asp Ser Gln Leu Arg Gly		
725	730	735
Leu Leu Ser Cys Arg Leu Ser Leu Leu Ser Tyr Thr Gly Thr Pro Thr		
740	745	750
Ala Ala Gly Val Ala Gln Gln Ala Arg Ala Trp Leu Thr Pro Val Gln		
755	760	765
Cys Tyr Asn Lys Ile Pro Trp Asp Val Met Lys Leu Asn Lys Ala Gly		
770	775	780
Phe Asn Val Pro Glu Ser Tyr Ser Leu Leu Lys Met Pro Pro Val Gly		
785	790	795
Cys Leu Ile Ser Ala Leu Lys Lys Ala Glu Asp Arg Gln Glu Val Ile		
805	810	815
Leu Arg Leu Phe Asn Pro Ala Glu Ser Ala Thr Cys Asp Ala Thr Val		
820	825	830
Ala Phe Ser Arg Glu Val Ile Ser Cys Ser Glu Thr Met Met Asp Glu		
835	840	845

His Ile Thr Thr Glu Glu Asn Gln Gly Ser Asn Leu Ser Gly Pro Phe  
 850 855 860  
 Leu Pro Gly Gln Ser Arg Thr Phe Ser Tyr Arg Leu Ala  
 865 870 875

<210> 354  
 <211> 523  
 <212> PRT  
 <213> E. Coli

<400> 354  
 Met Met Leu Asp Ile Val Glu Leu Ser Arg Leu Gln Phe Ala Leu Thr  
 1 5 10 15  
 Ala Met Tyr His Phe Leu Phe Val Pro Leu Thr Leu Gly Met Ala Phe  
 20 25 30  
 Leu Leu Ala Ile Met Glu Thr Val Tyr Val Leu Ser Gly Lys Gln Ile  
 35 40 45  
 Tyr Lys Asp Met Thr Lys Phe Trp Gly Lys Leu Phe Gly Ile Asn Phe  
 50 55 60  
 Ala Leu Gly Val Ala Thr Gly Leu Thr Met Glu Phe Gln Phe Gly Thr  
 65 70 75 80  
 Asn Trp Ser Tyr Tyr Ser His Tyr Val Gly Asp Ile Phe Gly Ala Pro  
 85 90 95  
 Leu Ala Ile Glu Gly Leu Met Ala Phe Phe Leu Glu Ser Thr Phe Val  
 100 105 110  
 Gly Leu Phe Phe Gly Trp Asp Arg Leu Gly Lys Val Gln His Met  
 115 120 125  
 Cys Val Thr Trp Leu Val Ala Leu Gly Ser Asn Leu Ser Ala Leu Trp  
 130 135 140  
 Ile Leu Val Ala Asn Gly Trp Met Gln Asn Pro Ile Ala Ser Asp Phe  
 145 150 155 160  
 Asn Phe Glu Thr Met Arg Met Glu Met Val Ser Phe Ser Glu Leu Val  
 165 170 175  
 Leu Asn Pro Val Ala Gln Val Lys Phe Val His Thr Val Ala Ser Gly  
 180 185 190  
 Tyr Val Thr Gly Ala Met Phe Ile Leu Gly Ile Ser Ala Trp Tyr Met  
 195 200 205  
 Leu Lys Gly Arg Asp Phe Ala Phe Ala Lys Arg Ser Phe Ala Ile Ala  
 210 215 220  
 Ala Ser Phe Gly Met Ala Ala Val Leu Ser Val Ile Val Leu Gly Asp  
 225 230 235 240  
 Glu Ser Gly Tyr Glu Met Gly Asp Val Gln Lys Thr Lys Leu Ala Ala  
 245 250 255  
 Ile Glu Ala Glu Trp Glu Thr Gln Pro Ala Pro Ala Ala Phe Thr Leu  
 260 265 270  
 Phe Gly Ile Pro Asp Gln Glu Glu Glu Thr Asn Lys Phe Ala Ile Gln  
 275 280 285  
 Ile Pro Tyr Ala Leu Gly Ile Ile Ala Thr Arg Ser Val Asp Thr Pro  
 290 295 300  
 Val Ile Gly Leu Lys Glu Leu Met Val Gln His Glu Glu Arg Ile Arg  
 305 310 315 320  
 Asn Gly Met Lys Ala Tyr Ser Leu Leu Glu Gln Leu Arg Ser Gly Ser  
 325 330 335  
 Thr Asp Gln Ala Val Arg Asp Gln Phe Asn Ser Met Lys Lys Asp Leu  
 340 345 350  
 Gly Tyr Gly Leu Leu Leu Lys Arg Tyr Thr Pro Asn Val Ala Asp Ala  
 355 360 365  
 Thr Glu Ala Gln Ile Gln Gln Ala Thr Lys Asp Ser Ile Pro Arg Val  
 370 375 380  
 Ala Pro Leu Tyr Phe Ala Phe Arg Ile Met Val Ala Cys Gly Phe Leu

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385          390          395          400
Leu Leu Ala Ile Ile Ala Leu Ser Phe Trp Ser Val Ile Arg Asn Arg
          405          410          415
Ile Gly Glu Lys Lys Trp Leu Leu Arg Ala Ala Leu Tyr Gly Ile Pro
          420          425          430
Leu Pro Trp Ile Ala Val Glu Ala Gly Trp Phe Val Ala Glu Tyr Gly
          435          440          445
Arg Gln Pro Trp Ala Ile Gly Glu Val Leu Pro Thr Ala Val Ala Asn
          450          455          460
Ser Ser Leu Thr Ala Gly Asp Leu Ile Phe Ser Met Val Leu Ile Cys
465          470          475          480
Gly Leu Tyr Thr Leu Phe Leu Val Ala Glu Leu Phe Leu Met Phe Lys
          485          490          495
Phe Ala Arg Leu Gly Pro Ser Ser Leu Lys Thr Gly Arg Tyr His Phe
          500          505          510
Glu Gln Ser Ser Thr Thr Thr Gln Pro Ala Arg
          515          520

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<210> 355  
 <211> 379  
 <212> PRT  
 <213> E. Coli

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<400> 355
Met Ile Asp Tyr Glu Val Leu Arg Phe Ile Trp Trp Leu Leu Val Gly
 1          5          10          15
Val Leu Leu Ile Gly Phe Ala Val Thr Asp Gly Phe Asp Met Gly Val
 20          25          30
Gly Met Leu Thr Arg Phe Leu Gly Arg Asn Asp Thr Glu Arg Arg Ile
 35          40          45
Met Ile Asn Ser Ile Ala Pro His Trp Asp Gly Asn Gln Val Trp Leu
 50          55          60
Ile Thr Ala Gly Gly Ala Leu Phe Ala Ala Trp Pro Met Val Tyr Ala
 65          70          75          80
Ala Ala Phe Ser Gly Phe Tyr Val Ala Met Ile Leu Val Leu Ala Ser
          85          90          95
Leu Phe Phe Arg Pro Val Gly Phe Asp Tyr Arg Ser Lys Ile Glu Glu
          100          105          110
Thr Arg Trp Arg Asn Met Trp Asp Trp Gly Ile Phe Ile Gly Ser Phe
          115          120          125
Val Pro Pro Leu Val Ile Gly Val Ala Phe Gly Asn Leu Leu Gln Gly
          130          135          140
Val Pro Phe Asn Val Asp Glu Tyr Leu Arg Leu Tyr Tyr Thr Gly Asn
 145          150          155          160
Phe Phe Gln Leu Leu Asn Pro Phe Gly Leu Leu Ala Gly Val Val Ser
          165          170          175
Val Gly Met Ile Ile Thr Gln Gly Ala Thr Tyr Leu Gln Met Arg Thr
          180          185          190
Val Gly Glu Leu His Leu Arg Thr Arg Ala Thr Ala Gln Val Ala Ala
          195          200          205
Leu Val Thr Leu Val Cys Phe Ala Leu Ala Gly Val Trp Val Met Tyr
 210          215          220
Gly Ile Asp Gly Tyr Val Val Lys Ser Thr Met Asp His Tyr Ala Ala
 225          230          235          240
Ser Asn Pro Leu Asn Lys Glu Val Val Arg Glu Ala Gly Ala Trp Leu
          245          250          255
Val Asn Phe Asn Asn Thr Pro Ile Leu Trp Ala Ile Pro Ala Leu Gly
          260          265          270
Val Val Leu Pro Leu Leu Thr Ile Leu Thr Ala Arg Met Asp Lys Ala
          275          280          285

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Ala Trp Ala Phe Val Phe Ser Ser Leu Thr Leu Ala Cys Ile Ile Leu  
 290 295 300  
 Thr Ala Gly Ile Ala Met Phe Pro Phe Val Met Pro Ser Ser Thr Met  
 305 310 315 320  
 Met Asn Ala Ser Leu Thr Met Trp Asp Ala Thr Ser Ser Gln Leu Thr  
 325 330 335  
 Leu Asn Val Met Thr Trp Val Ala Val Val Leu Val Pro Ile Ile Leu  
 340 345 350  
 Leu Tyr Thr Ala Trp Cys Tyr Trp Lys Met Phe Gly Arg Ile Thr Lys  
 355 360 365  
 Glu Asp Ile Glu Arg Asn Thr His Ser Leu Tyr  
 370 375

<210> 356  
 <211> 456  
 <212> PRT  
 <213> E. Coli

<400> 356  
 Met Glu Leu Ser Ser Leu Thr Ala Val Ser Pro Val Asp Gly Arg Tyr  
 1 5 10 15  
 Gly Asp Lys Val Ser Ala Leu Arg Gly Ile Phe Ser Glu Tyr Gly Leu  
 20 25 30  
 Leu Lys Phe Arg Val Gln Val Glu Val Arg Trp Leu Gln Lys Leu Ala  
 35 40 45  
 Ala His Ala Ala Ile Lys Glu Val Pro Ala Phe Ala Ala Asp Ala Ile  
 50 55 60  
 Gly Tyr Leu Asp Ala Ile Val Ala Ser Phe Ser Glu Glu Asp Ala Ala  
 65 70 75 80  
 Arg Ile Lys Thr Ile Glu Arg Thr Thr Asn His Asp Val Lys Ala Val  
 85 90 95  
 Glu Tyr Phe Leu Lys Glu Lys Val Ala Glu Ile Pro Glu Leu His Ala  
 100 105 110  
 Val Ser Glu Phe Ile His Phe Ala Cys Thr Ser Glu Asp Ile Asn Asn  
 115 120 125  
 Leu Ser His Ala Leu Met Leu Lys Thr Ala Arg Asp Glu Val Ile Leu  
 130 135 140  
 Pro Tyr Trp Arg Gln Leu Ile Asp Gly Ile Lys Asp Leu Ala Val Gln  
 145 150 155 160  
 Tyr Arg Asp Ile Pro Leu Leu Ser Arg Thr His Gly Gln Pro Ala Thr  
 165 170 175  
 Pro Ser Thr Ile Gly Lys Glu Met Ala Asn Val Ala Tyr Arg Met Glu  
 180 185 190  
 Arg Gln Tyr Arg Gln Leu Asn Gln Val Glu Ile Leu Gly Lys Ile Asn  
 195 200 205  
 Gly Ala Val Gly Asn Tyr Asn Ala His Ile Ala Ala Tyr Pro Glu Val  
 210 215 220  
 Asp Trp His Gln Phe Ser Glu Glu Phe Val Thr Ser Leu Gly Ile Gln  
 225 230 235 240  
 Trp Asn Pro Tyr Thr Gln Ile Glu Pro His Asp Tyr Ile Ala Glu  
 245 250 255  
 Leu Phe Asp Cys Val Ala Arg Phe Asn Thr Ile Leu Ile Asp Phe Asp  
 260 265 270  
 Arg Asp Val Trp Gly Tyr Ile Ala Leu Asn His Phe Lys Gln Lys Thr  
 275 280 285  
 Ile Ala Gly Glu Ile Gly Ser Ser Thr Met Pro His Lys Val Asn Pro  
 290 295 300  
 Ile Asp Phe Glu Asn Ser Glu Gly Asn Leu Gly Leu Ser Asn Ala Val  
 305 310 315 320  
 Leu Gln His Leu Ala Ser Lys Leu Pro Val Ser Arg Trp Gln Arg Asp

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          325          330          335
Leu Thr Asp Ser Thr Val Leu Arg Asn Leu Gly Val Gly Ile Gly Tyr
          340          345          350
Ala Leu Ile Ala Tyr Gln Ser Thr Leu Lys Gly Val Ser Lys Leu Glu
          355          360          365
Val Asn Arg Asp His Leu Leu Asp Glu Leu Asp His Asn Trp Glu Val
          370          375          380
Leu Ala Glu Pro Ile Gln Thr Val Met Arg Arg Tyr Gly Ile Glu Lys
          385          390          395          400
Pro Tyr Glu Lys Leu Lys Glu Leu Thr Arg Gly Lys Arg Val Asp Ala
          405          410          415
Glu Gly Met Lys Gln Phe Ile Asp Gly Leu Ala Leu Pro Glu Glu Glu
          420          425          430
Lys Ala Arg Leu Lys Ala Met Thr Pro Ala Asn Tyr Ile Gly Arg Ala
          435          440          445
Ile Thr Met Val Asp Glu Leu Lys
          450          455

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<210> 357  
 <211> 61  
 <212> PRT  
 <213> E. Coli

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          <400> 357
Met Leu Ile Leu Thr Arg Arg Val Gly Glu Thr Leu Met Ile Gly Asp
  1          5          10          15
Glu Val Thr Val Thr Val Leu Gly Val Lys Gly Asn Gln Val Arg Ile
          20          25          30
Gly Val Asn Ala Pro Lys Glu Val Ser Val His Arg Glu Glu Ile Tyr
          35          40          45
Gln Arg Ile Gln Ala Glu Lys Ser Gln Gln Ser Ser Tyr
          50          55          60

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<210> 358  
 <211> 83  
 <212> RNA  
 <213> E. Coli

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          <400> 358
ggugaggugg ccgagaggcu gaaggcgcuc ccugcuaag ggaguaugcg gucaaaagcu
gcauccgggg uucgaauccc cgccuaccg cca

```

60  
83

<210> 359  
 <211> 200  
 <212> PRT  
 <213> E. Coli

```

          <400> 359
Met Lys Asn Lys Ala Asp Asn Lys Lys Arg Asn Phe Leu Thr His Ser
  1          5          10          15
Glu Ile Glu Ser Leu Leu Lys Ala Ala Asn Thr Gly Pro His Ala Ala
          20          25          30
Arg Asn Tyr Cys Leu Thr Leu Leu Cys Phe Ile His Gly Phe Arg Ala
          35          40          45
Ser Glu Ile Cys Arg Leu Arg Ile Ser Asp Ile Asp Leu Lys Ala Lys
          50          55          60
Cys Ile Tyr Ile His Arg Leu Lys Lys Gly Phe Ser Thr Thr His Pro
          65          70          75          80

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Leu Leu Asn Lys Glu Val Gln Ala Leu Lys Asn Trp Leu Ser Ile Arg  
                     85                    90                    95  
 Thr Ser Tyr Pro His Ala Glu Ser Glu Trp Val Phe Leu Ser Arg Lys  
                     100                    105                    110  
 Gly Asn Pro Leu Ser Arg Gln Gln Phe Tyr His Ile Ile Ser Thr Ser  
                     115                    120                    125  
 Gly Gly Asn Ala Gly Leu Ser Leu Glu Ile His Pro His Met Leu Arg  
                     130                    135                    140  
 His Ser Cys Gly Phe Ala Leu Ala Asn Met Gly Ile Asp Thr Arg Leu  
 145                    150                    155                    160  
 Ile Gln Asp Tyr Leu Gly His Arg Asn Ile Arg His Thr Val Trp Tyr  
                     165                    170                    175  
 Thr Ala Ser Asn Ala Gly Arg Phe Tyr Gly Ile Trp Asp Arg Ala Arg  
                     180                    185                    190  
 Gly Arg Gln Arg His Ala Val Leu  
                     195                    200

<210> 360  
 <211> 198  
 <212> PRT  
 <213> E. Coli

<400> 360  
 Met Ser Lys Arg Arg Tyr Leu Thr Gly Lys Glu Val Gln Ala Met Met  
 1                    5                    10                    15  
 Gln Ala Val Cys Tyr Gly Ala Thr Gly Ala Arg Asp Tyr Cys Leu Ile  
                     20                    25                    30  
 Leu Leu Ala Tyr Arg His Gly Met Arg Ile Ser Glu Leu Leu Asp Leu  
                     35                    40                    45  
 His Tyr Gln Asp Leu Asp Leu Asn Glu Gly Arg Ile Asn Ile Arg Arg  
 50                    55                    60  
 Leu Lys Asn Gly Phe Ser Thr Val His Pro Leu Arg Phe Asp Glu Arg  
 65                    70                    75                    80  
 Glu Ala Val Glu Arg Trp Thr Gln Glu Arg Ala Asn Trp Lys Gly Ala  
                     85                    90                    95  
 Asp Arg Thr Asp Ala Ile Phe Ile Ser Arg Arg Gly Ser Arg Leu Ser  
                     100                    105                    110  
 Arg Gln Gln Ala Tyr Arg Ile Ile Arg Asp Ala Gly Ile Glu Ala Gly  
                     115                    120                    125  
 Thr Val Thr Gln Thr His Pro His Met Leu Arg His Ala Cys Gly Tyr  
                     130                    135                    140  
 Glu Leu Ala Glu Arg Gly Ala Asp Thr Arg Leu Ile Gln Asp Tyr Leu  
 145                    150                    155                    160  
 Gly His Arg Asn Ile Arg His Thr Val Arg Tyr Thr Ala Ser Asn Ala  
                     165                    170                    175  
 Ala Arg Phe Ala Gly Leu Trp Glu Arg Asn Asn Leu Ile Asn Glu Lys  
                     180                    185                    190  
 Leu Lys Arg Glu Glu Val  
                     195

<210> 361  
 <211> 182  
 <212> PRT  
 <213> E. Coli

<400> 361  
 Met Lys Ile Lys Thr Leu Ala Ile Val Val Leu Ser Ala Leu Ser Leu  
 1                    5                    10                    15

Ser Ser Thr Ala Ala Leu Ala Ala Thr Thr Val Asn Gly Gly Thr  
 20 25 30  
 Val His Phe Lys Gly Glu Val Val Asn Ala Ala Cys Ala Val Asp Ala  
 35 40 45  
 Gly Ser Val Asp Gln Thr Val Gln Leu Gly Gln Val Arg Thr Ala Ser  
 50 55 60  
 Leu Ala Gln Glu Gly Ala Thr Ser Ser Ala Val Gly Phe Asn Ile Gln  
 65 70 75 80  
 Leu Asn Asp Cys Asp Thr Asn Val Ala Ser Lys Ala Ala Val Ala Phe  
 85 90 95  
 Leu Gly Thr Ala Ile Asp Ala Gly His Thr Asn Val Leu Ala Leu Gln  
 100 105 110  
 Ser Ser Ala Ala Gly Ser Ala Thr Asn Val Gly Val Gln Ile Leu Asp  
 115 120 125  
 Arg Thr Gly Ala Ala Leu Thr Leu Asp Gly Ala Thr Phe Ser Ser Glu  
 130 135 140  
 Thr Thr Leu Asn Asn Gly Thr Asn Thr Ile Pro Phe Gln Ala Arg Tyr  
 145 150 155 160  
 Phe Ala Thr Gly Ala Ala Thr Pro Gly Ala Ala Asn Ala Asp Ala Thr  
 165 170 175  
 Phe Lys Val Gln Tyr Gln  
 180

<210> 362  
 <211> 215  
 <212> PRT  
 <213> E. Coli

<400> 362  
 Met Leu Leu Met Arg Met Arg Pro Ser Arg Phe Ser Ile Asn Asn Leu  
 1 5 10 15  
 Pro Arg Phe Arg Asp Val Ile Thr Gly Arg Asp Ala His Pro Cys Ala  
 20 25 30  
 Ile Lys Ile Thr Met Lys Arg Lys Arg Leu Phe Leu Leu Ala Ser Leu  
 35 40 45  
 Leu Pro Met Phe Ala Leu Ala Gly Asn Lys Trp Asn Thr Thr Leu Pro  
 50 55 60  
 Gly Gly Asn Met Gln Phe Gln Gly Val Ile Ile Ala Glu Thr Cys Arg  
 65 70 75 80  
 Ile Glu Ala Gly Asp Lys Gln Met Thr Val Asn Met Gly Gln Ile Ser  
 85 90 95  
 Ser Asn Arg Phe His Ala Val Gly Glu Asp Ser Ala Pro Val Pro Phe  
 100 105 110  
 Val Ile His Leu Arg Glu Cys Ser Thr Val Val Ser Glu Arg Val Gly  
 115 120 125  
 Val Ala Phe His Gly Val Ala Asp Gly Lys Asn Pro Asp Val Leu Ser  
 130 135 140  
 Val Gly Glu Gly Pro Gly Ile Ala Thr Asn Ile Gly Val Ala Leu Phe  
 145 150 155 160  
 Asp Asp Glu Gly Asn Leu Val Pro Ile Asn Arg Pro Pro Ala Asn Trp  
 165 170 175  
 Lys Arg Leu Tyr Ser Gly Ser Thr Ser Leu His Phe Ile Ala Lys Tyr  
 180 185 190  
 Arg Ala Thr Gly Arg Arg Val Thr Gly Gly Ile Ala Asn Ala Gln Ala  
 195 200 205  
 Trp Phe Ser Leu Thr Tyr Gln  
 210 215

<210> 363  
 <211> 241  
 <212> PRT  
 <213> E. Coli

<400> 363  
 Met Ser Asn Lys Asn Val Asn Val Arg Lys Ser Gln Glu Ile Thr Phe  
 1 5 10 15  
 Cys Leu Leu Ala Gly Ile Leu Met Phe Met Ala Met Met Val Ala Gly  
 20 25 30  
 Arg Ala Glu Ala Gly Val Ala Leu Gly Ala Thr Arg Val Ile Tyr Pro  
 35 40 45  
 Ala Gly Gln Lys Gln Glu Gln Leu Ala Val Thr Asn Asn Asp Glu Asn  
 50 55 60  
 Ser Thr Tyr Leu Ile Gln Ser Trp Val Glu Asn Ala Asp Gly Val Lys  
 65 70 75 80  
 Asp Gly Arg Phe Ile Val Thr Pro Pro Leu Phe Ala Met Lys Gly Lys  
 85 90 95  
 Lys Glu Asn Thr Leu Arg Ile Leu Asp Ala Thr Asn Asn Gln Leu Pro  
 100 105 110  
 Gln Asp Arg Glu Ser Leu Phe Trp Met Asn Val Lys Ala Ile Pro Ser  
 115 120 125  
 Met Asp Lys Ser Lys Leu Thr Glu Asn Thr Leu Gln Leu Ala Ile Ile  
 130 135 140  
 Ser Arg Ile Lys Leu Tyr Tyr Arg Pro Ala Lys Leu Ala Leu Pro Pro  
 145 150 155 160  
 Asp Gln Ala Ala Glu Lys Leu Arg Phe Arg Arg Ser Ala Asn Ser Leu  
 165 170 175  
 Thr Leu Ile Asn Pro Thr Pro Tyr Tyr Leu Thr Val Thr Glu Leu Asn  
 180 185 190  
 Ala Gly Thr Arg Val Leu Glu Asn Ala Leu Val Pro Pro Met Gly Glu  
 195 200 205  
 Ser Thr Val Lys Leu Pro Ser Asp Ala Gly Ser Asn Ile Thr Tyr Arg  
 210 215 220  
 Thr Ile Asn Asp Tyr Gly Ala Leu Thr Pro Lys Met Thr Gly Val Met  
 225 230 235 240  
 Glu

<210> 364  
 <211> 878  
 <212> PRT  
 <213> E. Coli

<400> 364  
 Met Ser Tyr Leu Asn Leu Arg Leu Tyr Gln Arg Asn Thr Gln Cys Leu  
 1 5 10 15  
 His Ile Arg Lys His Arg Leu Ala Gly Phe Phe Val Arg Leu Val Val  
 20 25 30  
 Ala Cys Ala Phe Ala Ala Gln Ala Pro Leu Ser Ser Ala Asp Leu Tyr  
 35 40 45  
 Phe Asn Pro Arg Phe Leu Ala Asp Asp Pro Gln Ala Val Ala Asp Leu  
 50 55 60  
 Ser Arg Phe Glu Asn Gly Gln Glu Leu Pro Pro Gly Thr Tyr Arg Val  
 65 70 75 80  
 Asp Ile Tyr Leu Asn Asn Gly Tyr Met Ala Thr Arg Asp Val Thr Phe  
 85 90 95  
 Asn Thr Gly Asp Ser Glu Gln Gly Ile Val Pro Cys Leu Thr Arg Ala  
 100 105 110  
 Gln Leu Ala Ser Met Gly Leu Asn Thr Ala Ser Val Ala Gly Met Asn

115	120	125
Leu Leu Ala Asp Asp Ala Cys Val Pro Leu Thr Thr Met Val Gln Asp		
130	135	140
Ala Thr Ala His Leu Asp Val Gly Gln Gln Arg Leu Asn Leu Thr Ile		
145	150	155
Pro Gln Ala Phe Met Ser Asn Arg Ala Arg Gly Tyr Ile Pro Pro Glu		
165	170	175
Leu Trp Asp Pro Gly Ile Asn Ala Gly Leu Leu Asn Tyr Asn Phe Ser		
180	185	190
Gly Asn Ser Val Gln Asn Arg Ile Gly Gly Asn Ser His Tyr Ala Tyr		
195	200	205
Leu Asn Leu Gln Ser Gly Leu Asn Ile Gly Ala Trp Arg Leu Arg Asp		
210	215	220
Asn Thr Thr Trp Ser Tyr Asn Ser Ser Asp Arg Ser Ser Gly Ser Lys		
225	230	235
Asn Lys Trp Gln His Ile Asn Thr Trp Leu Glu Arg Asp Ile Ile Pro		
245	250	255
Leu Arg Ser Arg Leu Thr Leu Gly Asp Gly Tyr Thr Gln Gly Asp Ile		
260	265	270
Phe Asp Gly Ile Asn Phe Arg Gly Ala Gln Leu Ala Ser Asp Asp Asn		
275	280	285
Met Leu Pro Asp Ser Gln Arg Gly Phe Ala Pro Val Ile His Gly Ile		
290	295	300
Ala Arg Gly Thr Ala Gln Val Thr Ile Lys Gln Asn Gly Tyr Asp Ile		
305	310	315
Tyr Asn Ser Thr Val Pro Pro Gly Pro Phe Thr Ile Asn Asp Ile Tyr		
325	330	335
Ala Ala Gly Asn Ser Gly Asp Leu Gln Val Thr Ile Lys Glu Ala Asp		
340	345	350
Gly Ser Thr Gln Ile Phe Thr Val Pro Tyr Ser Ser Val Pro Leu Leu		
355	360	365
Gln Arg Glu Gly His Thr Arg Tyr Ser Ile Thr Ala Gly Glu Tyr Arg		
370	375	380
Ser Gly Asn Ala Gln Gln Glu Lys Thr Arg Phe Phe Gln Ser Thr Leu		
385	390	395
Leu His Gly Leu Pro Ala Gly Trp Thr Ile Tyr Gly Gly Thr Gln Leu		
405	410	415
Ala Asp Arg Tyr Arg Ala Phe Asn Phe Gly Ile Gly Lys Asn Met Gly		
420	425	430
Ala Leu Gly Ala Leu Ser Val Asp Met Thr Gln Ala Asn Ser Thr Leu		
435	440	445
Pro Asp Asp Ser Gln His Asp Gly Gln Ser Val Arg Phe Leu Tyr Asn		
450	455	460
Lys Ser Leu Asn Glu Ser Gly Thr Asn Ile Gln Leu Val Gly Tyr Arg		
465	470	475
Tyr Ser Thr Ser Gly Tyr Phe Asn Phe Ala Asp Thr Thr Tyr Ser Arg		
485	490	495
Met Asn Gly Tyr Asn Ile Glu Thr Gln Asp Gly Val Ile Gln Val Lys		
500	505	510
Pro Lys Phe Thr Asp Tyr Tyr Asn Leu Ala Tyr Asn Lys Arg Gly Lys		
515	520	525
Leu Gln Leu Thr Val Thr Gln Gln Leu Gly Arg Thr Ser Thr Leu Tyr		
530	535	540
Leu Ser Gly Ser His Gln Thr Tyr Trp Gly Thr Ser Asn Val Asp Glu		
545	550	555
Gln Phe Gln Ala Gly Leu Asn Thr Ala Phe Glu Asp Ile Asn Trp Thr		
565	570	575
Leu Ser Tyr Ser Leu Thr Lys Asn Ala Trp Gln Lys Gly Arg Asp Gln		
580	585	590
Met Leu Ala Leu Asn Val Asn Ile Pro Phe Ser His Trp Leu Arg Ser		
595	600	605

Asp Ser Lys Ser Gln Trp Arg His Ala Ser Ala Ser Tyr Ser Met Ser  
 610 615 620  
 His Asp Leu Asn Gly Arg Met Thr Asn Leu Ala Gly Val Tyr Gly Thr  
 625 630 635 640  
 Leu Leu Glu Asp Asn Asn Leu Ser Tyr Ser Val Gln Thr Gly Tyr Ala  
 645 650 655  
 Gly Gly Gly Asp Gly Asn Ser Gly Ser Thr Gly Tyr Ala Thr Leu Asn  
 660 665 670  
 Tyr Arg Gly Gly Tyr Gly Asn Ala Asn Ile Gly Tyr Ser His Ser Asp  
 675 680 685  
 Asp Ile Lys Gln Leu Tyr Tyr Gly Val Ser Gly Gly Val Leu Ala His  
 690 695 700  
 Ala Asn Gly Val Thr Leu Gly Gln Pro Leu Asn Asp Thr Val Val Leu  
 705 710 715 720  
 Val Lys Ala Pro Gly Ala Lys Asp Ala Lys Val Glu Asn Gln Thr Gly  
 725 730 735  
 Val Arg Thr Asp Trp Arg Gly Tyr Ala Val Leu Pro Tyr Ala Thr Glu  
 740 745 750  
 Tyr Arg Glu Asn Arg Val Ala Leu Asp Thr Asn Thr Leu Ala Asp Asn  
 755 760 765  
 Val Asp Leu Asp Asn Ala Val Ala Asn Val Val Pro Thr Arg Gly Ala  
 770 775 780  
 Ile Val Arg Ala Glu Phe Lys Ala Arg Val Gly Ile Lys Leu Leu Met  
 785 790 795 800  
 Thr Leu Thr His Asn Asn Lys Pro Leu Pro Phe Gly Ala Met Val Thr  
 805 810 815  
 Ser Glu Ser Ser Gln Ser Ser Gly Ile Val Ala Asp Asn Gly Gln Val  
 820 825 830  
 Tyr Leu Ser Gly Met Pro Leu Ala Gly Lys Val Gln Val Lys Trp Gly  
 835 840 845  
 Glu Glu Glu Asn Ala His Cys Val Ala Asn Tyr Gln Leu Pro Pro Glu  
 850 855 860  
 Ser Gln Gln Gln Leu Leu Thr Gln Leu Ser Ala Glu Cys Arg  
 865 870 875

<210> 365  
 <211> 176  
 <212> PRT  
 <213> E. Coli

<400> 365  
 Met Arg Asn Lys Pro Phe Tyr Leu Leu Cys Ala Phe Leu Trp Leu Ala  
 1 5 10 15  
 Val Ser His Ala Leu Ala Ala Asp Ser Thr Ile Thr Ile Arg Gly Tyr  
 20 25 30  
 Val Arg Asp Asn Gly Cys Ser Val Ala Ala Glu Ser Thr Asn Phe Thr  
 35 40 45  
 Val Asp Leu Met Glu Asn Ala Ala Lys Gln Phe Asn Asn Ile Gly Ala  
 50 55 60  
 Thr Thr Pro Val Val Pro Phe Arg Ile Leu Leu Ser Pro Cys Gly Asn  
 65 70 75 80  
 Ala Val Ser Ala Val Lys Val Gly Phe Thr Gly Val Ala Asp Ser His  
 85 90 95  
 Asn Ala Asn Leu Leu Ala Leu Glu Asn Thr Val Ser Ala Ala Ser Gly  
 100 105 110  
 Leu Gly Ile Gln Leu Leu Asn Glu Gln Gln Asn Gln Ile Pro Leu Asn  
 115 120 125  
 Ala Pro Ser Ser Ala Leu Ser Trp Thr Thr Leu Thr Pro Gly Lys Pro  
 130 135 140  
 Asn Thr Leu Asn Phe Tyr Ala Arg Leu Met Ala Thr Gln Val Pro Val

145 150 155 160  
 Thr Ala Gly His Ile Asn Ala Thr Ala Thr Phe Thr Leu Glu Tyr Gln  
 165 170 175

<210> 366  
 <211> 167  
 <212> PRT  
 <213> E. Coli

<400> 366  
 Met Lys Trp Cys Lys Arg Gly Tyr Val Leu Ala Ala Ile Leu Ala Leu  
 1 5 10 15  
 Ala Ser Ala Thr Ile Gln Ala Ala Asp Val Thr Ile Thr Val Asn Gly  
 20 25 30  
 Lys Val Val Ala Lys Pro Cys Thr Val Ser Thr Thr Asn Ala Thr Val  
 35 40 45  
 Asp Leu Gly Asp Leu Tyr Ser Phe Ser Leu Met Ser Ala Gly Ala Ala  
 50 55 60  
 Ser Ala Trp His Asp Val Ala Leu Glu Leu Thr Asn Cys Pro Val Gly  
 65 70 75 80  
 Thr Ser Arg Val Thr Ala Ser Phe Ser Gly Ala Ala Asp Ser Thr Gly  
 85 90 95  
 Tyr Tyr Lys Asn Gln Gly Thr Ala Gln Asn Ile Gln Leu Glu Leu Gln  
 100 105 110  
 Asp Asp Ser Gly Asn Thr Leu Asn Thr Gly Ala Thr Lys Thr Val Gln  
 115 120 125  
 Val Asp Asp Ser Ser Gln Ser Ala His Phe Pro Leu Gln Val Arg Ala  
 130 135 140  
 Leu Thr Val Asn Gly Gly Ala Thr Gln Gly Thr Ile Gln Ala Val Ile  
 145 150 155 160  
 Ser Ile Thr Tyr Thr Tyr Ser  
 165

<210> 367  
 <211> 300  
 <212> PRT  
 <213> E. Coli

<400> 367  
 Met Lys Arg Val Ile Thr Leu Phe Ala Val Leu Leu Met Gly Trp Ser  
 1 5 10 15  
 Val Asn Ala Trp Ser Phe Ala Cys Lys Thr Ala Asn Gly Thr Ala Ile  
 20 25 30  
 Pro Ile Gly Gly Gly Ser Ala Asn Val Tyr Val Asn Leu Ala Pro Val  
 35 40 45  
 Val Asn Val Gly Gln Asn Leu Val Val Asp Leu Ser Thr Gln Ile Phe  
 50 55 60  
 Cys His Asn Asp Tyr Pro Glu Thr Ile Thr Asp Tyr Val Thr Leu Gln  
 65 70 75 80  
 Arg Gly Ser Ala Tyr Gly Gly Val Leu Ser Asn Phe Ser Gly Thr Val  
 85 90 95  
 Lys Tyr Ser Gly Ser Ser Tyr Pro Phe Pro Thr Thr Ser Glu Thr Pro  
 100 105 110  
 Arg Val Val Tyr Asn Ser Arg Thr Asp Lys Pro Trp Pro Val Ala Leu  
 115 120 125  
 Tyr Leu Thr Pro Val Ser Ser Ala Gly Gly Val Ala Ile Lys Ala Gly  
 130 135 140



Ser Leu Ile Ala Val Leu Ile Leu Arg Gln Thr Asn Asn Tyr Asn Ser  
 145 150 155 160  
 Asp Asp Phe Gln Phe Val Trp Asn Ile Tyr Ala Asn Asn Asp Val Val  
 165 170 175  
 Val Pro Thr Gly Gly Cys Asp Val Ser Ala Arg Asp Val Thr Val Thr  
 180 185 190  
 Leu Pro Asp Tyr Pro Gly Ser Val Pro Ile Pro Leu Thr Val Tyr Cys  
 195 200 205  
 Ala Lys Ser Gln Asn Leu Gly Tyr Tyr Leu Ser Gly Thr Thr Ala Asp  
 210 215 220  
 Ala Gly Asn Ser Ile Phe Thr Asn Thr Ala Ser Phe Ser Pro Ala Gln  
 225 230 235 240  
 Gly Val Gly Val Gln Leu Thr Arg Asn Gly Thr Ile Ile Pro Ala Asn  
 245 250 255  
 Asn Thr Val Ser Leu Gly Ala Val Gly Thr Ser Ala Val Ser Leu Gly  
 260 265 270  
 Leu Thr Ala Asn Tyr Ala Arg Thr Gly Gly Gln Val Thr Ala Gly Asn  
 275 280 285  
 Val Gln Ser Ile Ile Gly Val Thr Phe Val Tyr Gln  
 290 295 300

<210> 368  
 <211> 521  
 <212> PRT  
 <213> E. Coli

<400> 368  
 Met Leu Ser Lys Leu Pro Arg Arg Leu Arg Ser Phe Gln Thr Tyr Cys  
 1 5 10 15  
 Thr Ile Arg Val His Arg Gly Glu Asp Met Lys Ser Met Asp Lys Leu  
 20 25 30  
 Thr Thr Gly Val Ala Tyr Gly Thr Ser Ala Gly Asn Ala Gly Phe Trp  
 35 40 45  
 Ala Leu Gln Leu Leu Asp Lys Val Thr Pro Ser Gln Trp Ala Ala Ile  
 50 55 60  
 Gly Val Leu Gly Ser Leu Val Phe Gly Leu Leu Thr Tyr Leu Thr Asn  
 65 70 75 80  
 Leu Tyr Phe Lys Ile Lys Glu Asp Arg Arg Lys Ala Ala Arg Gly Glu  
 85 90 95  
 Ser Asn Asp Ser Arg Leu Thr Gly Cys Glu Arg Ser Pro Phe Glu Ser  
 100 105 110  
 Tyr Gly Asn Cys Ser Leu Thr Gly Gln Arg Thr Leu Arg Asn Phe Pro  
 115 120 125  
 Gly Cys Arg His Gly Pro Cys Arg Ser Cys Ala Gly Val Leu Gly Ser  
 130 135 140  
 Ser Gln Lys Glu Arg Pro Ala Ser Leu Pro Gly Ser Ser Arg Lys Ile  
 145 150 155 160  
 Val Arg Lys Ser Val Leu Ser Ala Ala Ser Val Leu Leu Asp Lys Ser  
 165 170 175  
 Cys Gln Ala Arg Ala Ser Ser Ser Ile Ser Met Asn Thr Lys Ile Arg  
 180 185 190  
 Tyr Gly Leu Ser Ala Ala Val Leu Ala Leu Ile Gly Ala Gly Ala Ser  
 195 200 205  
 Ala Pro Gln Ile Leu Asp Gln Phe Leu Asp Glu Lys Glu Gly Asn His  
 210 215 220  
 Thr Met Ala Tyr Arg Asp Gly Ser Gly Ile Trp Thr Ile Cys Arg Gly  
 225 230 235 240  
 Ala Thr Val Val Asp Gly Lys Thr Val Phe Pro Asn Met Lys Leu Ser  
 245 250 255

Lys Glu Lys Cys Asp Gln Val Asn Ala Ile Glu Arg Asp Lys Ala Leu  
 260 265 270  
 Ala Trp Val Glu Arg Asn Ile Lys Val Pro Leu Thr Glu Pro Gln Lys  
 275 280 285  
 Ala Gly Ile Ala Ser Phe Cys Pro Tyr Asn Ile Gly Pro Gly Lys Cys  
 290 295 300  
 Phe Pro Ser Thr Phe Tyr Lys Arg Leu Asn Ala Gly Asp Arg Lys Gly  
 305 310 315 320  
 Ala Cys Glu Ala Ile Arg Trp Trp Ile Lys Asp Gly Gly Arg Asp Cys  
 325 330 335  
 Arg Ile Arg Ser Asn Asn Cys Tyr Gly Gln Val Ile Arg Arg Asp Gln  
 340 345 350  
 Glu Ser Ala Leu Thr Cys Trp Gly Ile Glu Gln Ile Arg Tyr Ser Trp  
 355 360 365  
 Phe Phe Ser Cys Cys Gln Asp Leu Ser Ser Glu Met Ser Gly Ala Thr  
 370 375 380  
 Glu Asp Gly Lys Lys Asn Gly Arg Asn Val Met Leu Pro His Tyr His  
 385 390 395 400  
 Lys Arg Met Leu Asn Leu Leu Leu Glu Leu Asn Arg Gly Glu Leu Pro  
 405 410 415  
 Val Met Arg Leu Leu Lys Met Arg Asn Arg Asn Leu Leu Lys Phe Leu  
 420 425 430  
 Pro Gly Leu Leu Ile Cys Leu Ile Val Leu Thr Ser Cys Val Pro Lys  
 435 440 445  
 Gln Lys Asn Met Pro Tyr Ala Leu Thr Gln Arg Ser Ile Pro Gln Ile  
 450 455 460  
 Leu Pro Leu Pro Ser Glu Ala Lys Gln Pro Lys Pro Pro Lys Glu Cys  
 465 470 475 480  
 Ser Pro Thr Cys Ser Glu Ile Leu Gln Gln Lys Leu Ser Phe Met Leu  
 485 490 495  
 Lys Leu Leu Thr Asn Ala Thr Ser Gln Glu Leu Val Asn Arg Ser Met  
 500 505 510  
 Asn Leu Glu Ile Lys Ser Ile Lys Cys  
 515 520

<210> 369  
 <211> 177  
 <212> PRT  
 <213> E. Coli

<400> 369  
 Met Asn Thr Lys Ile Arg Tyr Gly Leu Ser Ala Ala Val Leu Ala Leu  
 1 5 10 15  
 Ile Gly Ala Gly Ala Ser Ala Pro Gln Ile Leu Asp Gln Phe Leu Asp  
 20 25 30  
 Glu Lys Glu Gly Asn His Thr Met Ala Tyr Arg Asp Gly Ser Gly Ile  
 35 40 45  
 Trp Thr Ile Cys Arg Gly Ala Thr Val Val Asp Gly Lys Thr Val Phe  
 50 55 60  
 Pro Asn Met Lys Leu Ser Lys Glu Lys Cys Asp Gln Val Asn Ala Ile  
 65 70 75 80  
 Glu Arg Asp Lys Ala Leu Ala Trp Val Glu Arg Asn Ile Lys Val Pro  
 85 90 95  
 Leu Thr Glu Pro Gln Lys Ala Gly Ile Ala Ser Phe Cys Pro Tyr Asn  
 100 105 110  
 Ile Gly Pro Gly Lys Cys Phe Pro Ser Thr Phe Tyr Lys Arg Leu Asn  
 115 120 125  
 Ala Gly Asp Arg Lys Gly Ala Cys Glu Ala Ile Arg Trp Trp Ile Lys  
 130 135 140

Asp Gly Gly Arg Asp Cys Arg Ile Arg Ser Asn Asn Cys Tyr Gly Gln  
 145 150 155 160  
 Val Ile Arg Arg Asp Gln Glu Ser Ala Leu Thr Cys Trp Gly Ile Glu  
 165 170 175  
 Gln

<210> 370  
 <211> 103  
 <212> PRT  
 <213> E. Coli

<400> 370  
 Met Thr Gln Asp Tyr Glu Leu Val Val Lys Gly Val Arg Asn Phe Glu  
 1 5 10 15  
 Asn Lys Val Thr Val Thr Val Ala Leu Gln Asp Lys Glu Arg Phe Asp  
 20 25 30  
 Gly Glu Ile Phe Asp Leu Asp Val Ala Met Asp Arg Val Glu Gly Ala  
 35 40 45  
 Ala Leu Glu Phe Tyr Glu Ala Ala Ala Arg Arg Ser Val Arg Gln Val  
 50 55 60  
 Phe Leu Glu Val Ala Glu Lys Leu Ser Glu Lys Val Glu Ser Tyr Leu  
 65 70 75 80  
 Gln His Gln Tyr Ser Phe Lys Ile Glu Asn Pro Ala Asn Lys His Glu  
 85 90 95  
 Arg Pro His His Lys Tyr Leu  
 100

<210> 371  
 <211> 96  
 <212> PRT  
 <213> E. Coli

<400> 371  
 Met Leu Ser Lys Leu Pro Arg Arg Leu Arg Ser Phe Gln Thr Tyr Cys  
 1 5 10 15  
 Thr Ile Arg Val His Arg Gly Glu Asp Met Lys Ser Met Asp Lys Leu  
 20 25 30  
 Thr Thr Gly Val Ala Tyr Gly Thr Ser Ala Gly Asn Ala Gly Phe Trp  
 35 40 45  
 Ala Leu Gln Leu Leu Asp Lys Val Thr Pro Ser Gln Trp Ala Ala Ile  
 50 55 60  
 Gly Val Leu Gly Ser Leu Val Phe Gly Leu Leu Thr Tyr Leu Thr Asn  
 65 70 75 80  
 Leu Tyr Phe Lys Ile Lys Glu Asp Arg Arg Lys Ala Ala Arg Gly Glu  
 85 90 95

<210> 372  
 <211> 71  
 <212> PRT  
 <213> E. Coli

<400> 372  
 Met Ser Asn Lys Met Thr Gly Leu Val Lys Trp Phe Asn Ala Asp Lys  
 1 5 10 15  
 Gly Phe Gly Phe Ile Ser Pro Val Asp Gly Ser Lys Asp Val Phe Val

20 25 30  
 His Phe Ser Ala Ile Gln Asn Asp Asn Tyr Arg Thr Leu Phe Glu Gly  
 35 40 45  
 Gln Lys Val Thr Phe Ser Ile Glu Ser Gly Ala Lys Gly Pro Ala Ala  
 50 55 60  
 Ala Asn Val Ile Ile Thr Asp  
 65 70

<210> 373  
 <211> 338  
 <212> PRT  
 <213> E. Coli

<400> 373  
 Met Phe Val Ile Trp Ser His Arg Thr Gly Phe Ile Met Ser His Gln  
 1 5 10 15  
 Leu Thr Phe Ala Asp Ser Glu Phe Ser Ser Lys Arg Arg Gln Thr Arg  
 20 25 30  
 Lys Glu Ile Phe Leu Ser Arg Met Glu Gln Ile Leu Pro Trp Gln Asn  
 35 40 45  
 Met Val Glu Val Ile Glu Pro Phe Tyr Pro Lys Ala Gly Asn Gly Arg  
 50 55 60  
 Arg Pro Tyr Pro Leu Glu Thr Met Leu Arg Ile His Cys Met Gln His  
 65 70 75 80  
 Trp Tyr Asn Leu Ser Asp Gly Ala Met Glu Asp Ala Leu Tyr Glu Ile  
 85 90 95  
 Ala Ser Met Arg Leu Phe Ala Arg Leu Ser Leu Asp Ser Ala Leu Pro  
 100 105 110  
 Asp Arg Thr Thr Ile Met Asn Phe Arg His Leu Leu Glu Gln His Gln  
 115 120 125  
 Leu Ala Arg Gln Leu Phe Lys Thr Ile Asn Arg Trp Leu Ala Glu Ala  
 130 135 140  
 Gly Val Met Met Thr Gln Gly Thr Leu Val Asp Ala Thr Ile Ile Glu  
 145 150 155 160  
 Ala Pro Ser Ser Thr Lys Asn Lys Glu Gln Gln Arg Asp Pro Glu Met  
 165 170 175  
 His Gln Thr Lys Lys Gly Asn Gln Trp His Phe Gly Met Lys Ala His  
 180 185 190  
 Ile Gly Val Asp Ala Lys Ser Gly Leu Thr His Ser Leu Val Thr Thr  
 195 200 205  
 Ala Ala Asn Glu His Asp Leu Asn Gln Leu Gly Asn Leu Leu His Gly  
 210 215 220  
 Glu Glu Gln Phe Val Ser Ala Asp Ala Gly Tyr Gln Gly Ala Pro Gln  
 225 230 235 240  
 Arg Glu Glu Leu Ala Glu Val Asp Val Asp Trp Leu Ile Ala Glu Arg  
 245 250 255  
 Pro Gly Lys Val Arg Thr Leu Lys Gln His Pro Arg Lys Asn Lys Thr  
 260 265 270  
 Ala Ile Asn Ile Glu Tyr Met Lys Ala Ser Ile Arg Ala Arg Val Glu  
 275 280 285  
 His Pro Phe Arg Ile Ile Lys Arg Gln Phe Gly Phe Val Lys Ala Arg  
 290 295 300  
 Tyr Lys Gly Leu Leu Lys Asn Asp Asn Gln Leu Ala Met Leu Phe Thr  
 305 310 315 320  
 Leu Ala Asn Leu Phe Arg Ala Asp Gln Met Ile Arg Gln Trp Glu Arg  
 325 330 335  
 Ser His

<210> 374  
 <211> 157  
 <212> PRT  
 <213> E. Coli

<400> 374  
 Met Val Tyr Ile Ile Ile Val Ser His Gly His Glu Asp Tyr Ile Lys  
 1 5 10 15  
 Lys Leu Leu Glu Asn Leu Asn Ala Asp Asp Glu His Tyr Lys Ile Ile  
 20 25 30  
 Val Arg Asp Asn Lys Asp Ser Leu Leu Lys Gln Ile Cys Gln His  
 35 40 45  
 Tyr Ala Gly Leu Asp Tyr Ile Ser Gly Gly Val Tyr Gly Phe Gly His  
 50 55 60  
 Asn Asn Asn Ile Ala Val Ala Tyr Val Lys Glu Lys Tyr Arg Pro Ala  
 65 70 75 80  
 Asp Asp Asp Tyr Ile Leu Phe Leu Asn Pro Asp Ile Ile Met Lys His  
 85 90 95  
 Asp Asp Leu Leu Thr Tyr Ile Lys Tyr Val Glu Ser Lys Arg Tyr Ala  
 100 105 110  
 Phe Ser Thr Leu Cys Leu Phe Arg Asp Glu Ala Lys Ser Leu His Asp  
 115 120 125  
 Tyr Ser Val Arg Lys Phe Pro Val Leu Ser Asp Phe Ile Val Ser Phe  
 130 135 140  
 Met Leu Gly Ile Lys Glu Gly Ala Asn Lys Ser Leu Ile  
 145 150 155

<210> 375  
 <211> 372  
 <212> PRT  
 <213> E. Coli

<400> 375  
 Met Gly Lys Ser Ile Val Val Val Ser Ala Val Asn Phe Thr Thr Gly  
 1 5 10 15  
 Gly Pro Phe Thr Ile Leu Lys Lys Phe Leu Ala Ala Thr Asn Lys  
 20 25 30  
 Glu Asn Val Ser Phe Ile Ala Leu Val His Ser Ala Lys Glu Leu Lys  
 35 40 45  
 Glu Ser Tyr Pro Trp Val Lys Phe Ile Glu Phe Pro Glu Val Lys Gly  
 50 55 60  
 Ser Trp Leu Lys Arg Leu His Phe Glu Tyr Val Val Cys Lys Lys Leu  
 65 70 75 80  
 Ser Lys Glu Leu Asn Ala Thr His Trp Ile Cys Leu His Asp Ile Thr  
 85 90 95  
 Ala Asn Val Val Thr Lys Lys Arg Tyr Val Tyr Cys His Asn Pro Ala  
 100 105 110  
 Pro Phe Tyr Lys Gly Ile Leu Phe Arg Glu Ile Leu Met Glu Pro Ser  
 115 120 125  
 Phe Phe Leu Phe Lys Met Leu Tyr Gly Leu Ile Tyr Lys Ile Asn Ile  
 130 135 140  
 Lys Lys Asn Thr Ala Val Phe Val Gln Gln Phe Trp Met Lys Glu Lys  
 145 150 155 160  
 Phe Ile Lys Lys Tyr Ser Ile Asn Asn Ile Ile Val Ser Arg Pro Glu  
 165 170 175  
 Ile Lys Leu Ser Asp Lys Ser Gln Leu Thr Asp Asp Asp Ser Gln Phe  
 180 185 190  
 Lys Asn Asn Pro Ser Glu Leu Thr Ile Phe Tyr Pro Ala Val Pro Arg

195 200 205  
 Val Phe Lys Asn Tyr Glu Leu Ile Ile Ser Ala Ala Arg Lys Leu Lys  
 210 215 220  
 Glu Gln Ser Asn Ile Lys Phe Leu Leu Thr Ile Ser Gly Thr Glu Asn  
 225 230 235 240  
 Ala Tyr Ala Lys Tyr Ile Ile Ser Leu Ala Glu Gly Leu Asp Asn Val  
 245 250 255  
 His Phe Leu Gly Tyr Leu Asp Lys Glu Lys Ile Asp His Cys Tyr Asn  
 260 265 270  
 Ile Ser Asp Ile Val Cys Phe Pro Ser Arg Leu Glu Thr Trp Gly Leu  
 275 280 285  
 Pro Leu Ser Glu Ala Lys Glu Arg Gly Lys Trp Val Leu Ala Ser Asp  
 290 295 300  
 Phe Pro Phe Thr Arg Glu Thr Leu Gly Ser Tyr Glu Lys Lys Ala Phe  
 305 310 315 320  
 Phe Asp Ser Asn Asn Asp Asp Met Leu Val Lys Leu Ile Ile Asp Phe  
 325 330 335  
 Lys Lys Gly Asn Leu Lys Lys Asp Ile Ser Asp Ala Asn Phe Ile Tyr  
 340 345 350  
 Arg Asn Glu Asn Val Leu Val Gly Phe Asp Glu Leu Val Asn Phe Ile  
 355 360 365  
 Thr Glu Glu His  
 370

<210> 376  
 <211> 196  
 <212> PRT  
 <213> E. Coli

<400> 376  
 Met Ile Leu Lys Leu Ala Lys Arg Tyr Gly Leu Cys Gly Phe Ile Arg  
 1 5 10 15  
 Leu Val Arg Asp Val Leu Leu Thr Arg Val Phe Tyr Arg Asn Cys Arg  
 20 25 30  
 Ile Ile Arg Phe Pro Cys Tyr Ile Arg Asn Asp Gly Ser Ile Asn Phe  
 35 40 45  
 Gly Glu Asn Phe Thr Ser Gly Val Gly Leu Arg Leu Asp Ala Phe Gly  
 50 55 60  
 Arg Gly Val Ile Phe Phe Ser Asp Asn Val Gln Val Asn Asp Tyr Val  
 65 70 75 80  
 His Ile Ala Ser Ile Glu Ser Val Thr Ile Gly Arg Asp Thr Leu Ile  
 85 90 95  
 Ala Ser Lys Val Phe Ile Thr Asp His Asn His Gly Ser Phe Lys His  
 100 105 110  
 Ser Asp Pro Met Ser Ser Pro Asn Ile Pro Pro Asp Met Arg Thr Leu  
 115 120 125  
 Glu Ser Ser Ala Val Val Ile Gly Gln Arg Val Trp Leu Gly Glu Asn  
 130 135 140  
 Val Thr Val Leu Pro Gly Thr Ile Ile Gly Asn Gly Val Val Val Gly  
 145 150 155 160  
 Ala Asn Ser Val Val Arg Gly Ser Ile Pro Glu Asn Thr Val Ile Ala  
 165 170 175  
 Gly Val Pro Ala Lys Ile Ile Lys Lys Tyr Asn His Glu Thr Lys Leu  
 180 185 190  
 Trp Glu Lys Ala  
 195

<210> 377  
 <211> 330  
 <212> PRT

&lt;213&gt; E. Coli

&lt;400&gt; 377

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Met Tyr Phe Leu Asn Asp Leu Asn Phe Ser Arg Arg Asp Ala Gly Phe
 1          5          10          15
Lys Ala Arg Lys Asp Ala Leu Asp Ile Ala Ser Asp Tyr Glu Asn Ile
          20          25          30
Ser Val Val Asn Ile Pro Leu Trp Gly Gly Val Val Gln Arg Ile Ile
          35          40          45
Ser Ser Val Lys Leu Ser Thr Phe Leu Cys Gly Leu Glu Asn Lys Asp
          50          55          60
Val Leu Ile Phe Asn Phe Pro Met Ala Lys Pro Phe Trp His Ile Leu
65          70          75          80
Ser Phe Phe His Arg Leu Leu Lys Phe Arg Ile Val Pro Leu Ile His
          85          90          95
Asp Ile Asp Glu Leu Arg Gly Gly Gly Gly Ser Asp Ser Val Arg Leu
          100          105          110
Ala Thr Cys Asp Met Val Ile Ser His Asn Pro Gln Met Thr Lys Tyr
          115          120          125
Leu Ser Lys Tyr Met Ser Gln Asp Lys Ile Lys Asp Ile Lys Ile Phe
          130          135          140
Asp Tyr Leu Val Ser Ser Asp Val Glu His Arg Asp Val Thr Asp Lys
145          150          155          160
Gln Arg Gly Val Ile Tyr Ala Gly Asn Leu Ser Arg His Lys Cys Ser
          165          170          175
Phe Ile Tyr Thr Glu Gly Cys Asp Phe Thr Leu Phe Gly Val Asn Tyr
          180          185          190
Glu Asn Lys Asp Asn Pro Lys Tyr Leu Gly Ser Phe Asp Ala Gln Ser
          195          200          205
Pro Glu Lys Ile Asn Leu Pro Gly Met Gln Phe Gly Leu Ile Trp Asp
          210          215          220
Gly Asp Ser Val Glu Thr Cys Ser Gly Ala Phe Gly Asp Tyr Leu Lys
225          230          235          240
Phe Asn Asn Pro His Lys Thr Ser Leu Tyr Leu Ser Met Glu Leu Pro
          245          250          255
Val Phe Ile Trp Asp Lys Ala Ala Leu Ala Asp Phe Ile Val Asp Asn
          260          265          270
Arg Ile Gly Tyr Ala Val Gly Ser Ile Lys Glu Met Gln Glu Ile Val
          275          280          285
Asp Ser Met Thr Ile Glu Thr Tyr Lys Gln Ile Ser Glu Asn Thr Lys
          290          295          300
Ile Ile Ser Gln Lys Ile Arg Thr Gly Ser Tyr Phe Arg Asp Val Leu
305          310          315          320
Glu Glu Val Ile Asp Asp Leu Lys Thr Arg
          325          330

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&lt;210&gt; 378

&lt;211&gt; 388

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 378

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Met Ile Tyr Leu Val Ile Ser Val Phe Leu Ile Thr Ala Phe Ile Cys
 1          5          10          15
Leu Tyr Leu Lys Lys Asp Ile Phe Tyr Pro Ala Val Cys Val Asn Ile
          20          25          30
Ile Phe Ala Leu Val Leu Leu Gly Tyr Glu Ile Thr Ser Asp Ile Tyr
          35          40          45
Ala Phe Gln Leu Asn Asp Ala Thr Leu Ile Phe Leu Leu Cys Asn Val
50          55          60

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Leu Thr Phe Thr Leu Ser Cys Leu Leu Thr Glu Ser Val Leu Asp Leu  
 65 70 75 80  
 Asn Ile Arg Lys Val Asn Asn Ala Ile Tyr Ser Ile Pro Ser Lys Lys  
 85 90 95  
 Val His Asn Val Gly Leu Leu Val Ile Ser Phe Ser Met Ile Tyr Ile  
 100 105 110  
 Cys Met Arg Leu Ser Asn Tyr Gln Phe Gly Thr Ser Leu Ser Tyr  
 115 120 125  
 Met Asn Leu Ile Arg Asp Ala Asp Val Glu Asp Thr Ser Arg Asn Phe  
 130 135 140  
 Ser Ala Tyr Met Gln Pro Ile Ile Leu Thr Thr Phe Ala Leu Phe Ile  
 145 150 155 160  
 Trp Ser Lys Lys Phe Thr Asn Thr Lys Val Ser Lys Thr Phe Thr Leu  
 165 170 175  
 Leu Val Phe Ile Val Phe Ile Phe Ala Ile Ile Leu Asn Thr Gly Lys  
 180 185 190  
 Gln Ile Val Phe Met Val Ile Ile Ser Tyr Ala Phe Ile Val Gly Val  
 195 200 205  
 Asn Arg Val Lys His Tyr Val Tyr Leu Ile Thr Ala Val Gly Val Leu  
 210 215 220  
 Phe Ser Leu Tyr Met Leu Phe Leu Arg Gly Leu Pro Gly Gly Met Ala  
 225 230 235 240  
 Tyr Tyr Leu Ser Met Tyr Leu Val Ser Pro Ile Ile Ala Phe Gln Glu  
 245 250 255  
 Phe Tyr Phe Gln Gln Val Ser Asn Ser Ala Ser Ser His Val Phe Trp  
 260 265 270  
 Phe Phe Glu Arg Leu Met Gly Leu Leu Thr Gly Gly Val Ser Met Ser  
 275 280 285  
 Leu His Lys Glu Phe Val Trp Val Gly Leu Pro Thr Asn Val Tyr Thr  
 290 295 300  
 Ala Phe Ser Asp Tyr Val Tyr Ile Ser Ala Glu Leu Ser Tyr Leu Met  
 305 310 315 320  
 Met Val Ile His Gly Cys Ile Ser Gly Val Leu Trp Arg Leu Ser Arg  
 325 330 335  
 Asn Tyr Ile Ser Val Lys Ile Phe Tyr Ser Tyr Phe Ile Tyr Thr Phe  
 340 345 350  
 Ser Phe Ile Phe Tyr His Glu Ser Phe Met Thr Asn Ile Ser Ser Trp  
 355 360 365  
 Ile Gln Ile Thr Leu Cys Ile Ile Val Phe Ser Gln Phe Leu Lys Ala  
 370 375 380  
 Gln Lys Ile Lys  
 385

&lt;210&gt; 379

&lt;211&gt; 367

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 379

Met Tyr Asp Tyr Ile Ile Val Gly Ser Gly Leu Phe Gly Ala Val Cys  
 1 5 10 15  
 Ala Asn Glu Leu Lys Lys Leu Asn Lys Lys Val Leu Val Ile Glu Lys  
 20 25 30  
 Arg Asn His Ile Gly Gly Asn Ala Tyr Thr Glu Asp Cys Glu Gly Ile  
 35 40 45  
 Gln Ile His Lys Tyr Gly Ala His Ile Phe His Thr Asn Asp Lys Tyr  
 50 55 60  
 Ile Trp Asp Tyr Val Asn Asp Leu Val Glu Phe Asn Arg Phe Thr Asn  
 65 70 75 80



Ser Pro Leu Ala Ile Tyr Lys Asp Lys Leu Phe Asn Leu Pro Phe Asn  
 85 90 95  
 Met Asn Thr Phe His Gln Met Trp Gly Val Lys Asp Pro Gln Glu Ala  
 100 105 110  
 Gln Asn Ile Ile Asn Ala Gln Lys Lys Tyr Gly Asp Lys Val Pro  
 115 120 125  
 Glu Asn Leu Glu Glu Gln Ala Ile Ser Leu Val Gly Glu Asp Leu Tyr  
 130 135 140  
 Gln Ala Leu Ile Lys Gly Tyr Thr Glu Lys Gln Trp Gly Arg Ser Ala  
 145 150 155 160  
 Lys Glu Leu Pro Ala Phe Ile Ile Lys Arg Ile Pro Val Arg Phe Thr  
 165 170 175  
 Phe Asp Asn Asn Tyr Phe Ser Asp Arg Tyr Gln Gly Ile Pro Val Gly  
 180 185 190  
 Gly Tyr Thr Lys Lys Leu Ile Glu Lys Met Leu Glu Gly Val Asp Val Lys  
 195 200 205  
 Leu Gly Ile Asp Phe Leu Lys Asp Lys Asp Ser Leu Ala Ser Lys Ala  
 210 215 220  
 His Arg Ile Ile Tyr Thr Gly Pro Ile Asp Gln Tyr Phe Asp Tyr Arg  
 225 230 235 240  
 Phe Gly Ala Leu Glu Tyr Arg Ser Leu Lys Phe Glu Thr Glu Arg His  
 245 250 255  
 Glu Phe Pro Asn Phe Gln Gly Asn Ala Val Ile Asn Phe Thr Asp Ala  
 260 265 270  
 Asn Val Pro Tyr Thr Arg Ile Ile Glu His Lys His Phe Asp Tyr Val  
 275 280 285  
 Glu Thr Lys His Thr Val Val Thr Lys Glu Tyr Pro Leu Glu Trp Lys  
 290 295 300  
 Val Gly Asp Glu Pro Tyr Tyr Pro Val Asn Asp Asn Lys Asn Met Glu  
 305 310 315 320  
 Leu Phe Lys Lys Tyr Arg Glu Leu Ala Ser Arg Glu Asp Lys Val Ile  
 325 330 335  
 Phe Gly Gly Arg Leu Ala Glu Tyr Lys Tyr Tyr Asp Met His Gln Val  
 340 345 350  
 Ile Ser Ala Ala Leu Tyr Gln Val Lys Asn Ile Met Ser Thr Asp  
 355 360 365

&lt;210&gt; 380

&lt;211&gt; 371

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 380

Met Phe Pro Lys Ile Met Asn Asp Glu Asn Phe Phe Lys Lys Ala Ala  
 1 5 10 15  
 Ala His Gly Glu Glu Pro Pro Leu Thr Pro Gln Asn Glu His Gln Arg  
 20 25 30  
 Ser Gly Leu Arg Phe Ala Arg Arg Val Arg Leu Pro Arg Ala Val Gly  
 35 40 45  
 Leu Ala Gly Met Phe Leu Pro Ile Ala Ser Thr Leu Val Ser His Pro  
 50 55 60  
 Pro Pro Gly Trp Trp Trp Leu Val Leu Val Gly Trp Ala Phe Val Trp  
 65 70 75 80  
 Pro His Leu Ala Trp Gln Ile Ala Ser Arg Ala Val Asp Pro Leu Ser  
 85 90 95  
 Arg Glu Ile Tyr Asn Leu Lys Thr Asp Ala Val Leu Ala Gly Met Trp  
 100 105 110  
 Val Gly Val Met Gly Val Asn Val Leu Pro Ser Thr Ala Met Leu Met  
 115 120 125  
 Ile Met Cys Leu Asn Leu Met Gly Ala Gly Gly Pro Arg Leu Phe Val

130 135 140  
 Ala Gly Leu Val Leu Met Val Val Ser Cys Leu Val Thr Leu Glu Leu  
 145 150 155 160  
 Thr Gly Ile Thr Val Ser Phe Asn Ser Ala Pro Leu Glu Trp Trp Leu  
 165 170 175  
 Ser Leu Pro Ile Ile Val Ile Tyr Pro Leu Leu Phe Gly Trp Val Ser  
 180 185 190  
 Tyr Gln Thr Ala Thr Lys Leu Ala Glu His Lys Arg Arg Leu Gln Val  
 195 200 205  
 Met Ser Thr Arg Asp Gly Met Thr Gly Val Tyr Asn Arg Arg His Trp  
 210 215 220  
 Glu Thr Met Leu Arg Asn Glu Phe Asp Asn Cys Arg Arg His Asn Arg  
 225 230 235 240  
 Asp Ala Thr Leu Leu Ile Ile Asp Ile Asp His Phe Lys Ser Ile Asn  
 245 250 255  
 Asp Thr Trp Gly His Asp Val Gly Asp Glu Ala Ile Val Ala Leu Thr  
 260 265 270  
 Arg Gln Leu Gln Ile Thr Leu Arg Gly Ser Asp Val Ile Gly Arg Phe  
 275 280 285  
 Gly Gly Asp Glu Phe Ala Val Ile Met Ser Gly Thr Pro Ala Glu Ser  
 290 295 300  
 Ala Ile Thr Ala Met Leu Arg Val His Glu Gly Leu Asn Thr Leu Arg  
 305 310 315 320  
 Leu Pro Asn Thr Pro Gln Val Thr Leu Arg Ile Ser Val Gly Val Ala  
 325 330 335  
 Pro Leu Asn Pro Gln Met Ser His Tyr Arg Glu Trp Leu Lys Ser Ala  
 340 345 350  
 Asp Leu Ala Leu Tyr Lys Ala Lys Lys Ala Gly Arg Asn Arg Thr Glu  
 355 360 365  
 Val Ala Ala  
 370

<210> 381  
 <211> 467  
 <212> PRT  
 <213> E. Coli

<400> 381  
 Met Asp Val Asn Val Asp Gln Phe Asp Thr Glu Ala Phe Arg Thr Asp  
 1 5 10 15  
 Lys Leu Glu Leu Thr Ser Gly Asn Ile Ala Asp His Asn Gly Asn Val  
 20 25 30  
 Val Ser Gly Val Phe Asp Ile His Ser Ser Asp Tyr Val Leu Asn Ala  
 35 40 45  
 Asp Leu Val Asn Asp Arg Thr Trp Asp Thr Ser Lys Ser Asn Tyr Gly  
 50 55 60  
 Tyr Gly Ile Val Ala Met Asn Ser Asp Gly His Leu Thr Ile Asn Gly  
 65 70 75 80  
 Asn Gly Asp Val Asp Asn Gly Thr Glu Leu Asp Asn Ser Ser Val Asp  
 85 90 95  
 Asn Val Val Ala Ala Thr Gly Asn Tyr Lys Val Arg Ile Asp Asn Ala  
 100 105 110  
 Thr Gly Ala Gly Ala Ile Ala Asp Tyr Lys Asp Lys Glu Ile Ile Tyr  
 115 120 125  
 Val Asn Asp Val Asn Ser Asn Ala Thr Phe Ser Ala Ala Asn Lys Ala  
 130 135 140  
 Asp Leu Gly Ala Tyr Thr Tyr Gln Ala Glu Gln Arg Gly Asn Thr Val  
 145 150 155 160  
 Val Leu Gln Gln Met Glu Leu Thr Asp Tyr Ala Asn Met Ala Leu Ser  
 165 170 175  
 Ile Pro Ser Ala Asn Thr Asn Ile Trp Asn Leu Glu Gln Asp Thr Val

180	185	190
Gly Thr Arg Leu Thr Asn Ser Arg His Gly Leu Ala Asp Asn Gly Gly		
195	200	205
Ala Trp Val Ser Tyr Phe Gly Gly Asn Phe Asn Gly Asp Asn Gly Thr		
210	215	220
Ile Asn Tyr Asp Gln Asp Val Asn Gly Ile Met Val Gly Val Asp Thr		
225	230	235
Lys Ile Asp Gly Asn Asn Ala Lys Trp Ile Val Gly Ala Ala Ala Gly		
245	250	255
Phe Ala Lys Gly Asp Met Asn Asp Arg Ser Gly Gln Val Asp Gln Asp		
260	265	270
Ser Gln Thr Ala Tyr Ile Tyr Ser Ser Ala His Phe Ala Asn Asn Val		
275	280	285
Phe Val Asp Gly Ser Leu Ser Tyr Ser His Phe Asn Asn Asp Leu Ser		
290	295	300
Ala Thr Met Ser Asn Gly Thr Tyr Val Asp Gly Ser Thr Asn Ser Asp		
305	310	315
Ala Trp Gly Phe Gly Leu Lys Ala Gly Tyr Asp Phe Lys Leu Gly Asp		
325	330	335
Ala Gly Tyr Val Thr Pro Tyr Gly Ser Val Ser Gly Leu Phe Gln Ser		
340	345	350
Gly Asp Asp Tyr Gln Leu Ser Asn Asp Met Lys Val Asp Gly Gln Ser		
355	360	365
Tyr Asp Ser Met Arg Tyr Glu Leu Gly Val Asp Ala Gly Tyr Thr Phe		
370	375	380
Thr Tyr Ser Glu Asp Gln Ala Leu Thr Pro Tyr Phe Lys Leu Ala Tyr		
385	390	395
Val Tyr Asp Asp Ser Asn Asn Asp Asn Val Asn Gly Asp Ser Ile		
405	410	415
Asp Asn Gly Thr Glu Gly Ser Ala Val Arg Val Gly Leu Gly Thr Gln		
420	425	430
Phe Ser Phe Thr Lys Asn Phe Ser Ala Tyr Thr Asp Ala Asn Tyr Leu		
435	440	445
Gly Gly Gly Asp Val Asp Gln Asp Trp Ser Ala Asn Val Gly Val Lys		
450	455	460
Tyr Thr Trp		
465		

<210> 382  
 <211> 222  
 <212> PRT  
 <213> E. Coli

<400> 382

Met Pro Val Lys Asp Leu Thr Gly Ile Thr Ala Lys Asp Ala Gln Met	
1 5 10 15	
Leu Ser Val Val Lys Pro Leu Gln Glu Phe Gly Lys Leu Asp Lys Cys	
20 25 30	
Leu Ser Arg Tyr Gly Thr Arg Phe Glu Phe Asn Asn Glu Lys Gln Val	
35 40 45	
Ile Phe Ser Ser Asp Val Asn Asn Glu Asp Thr Phe Val Ile Leu Glu	
50 55 60	
Gly Val Ile Ser Leu Arg Glu Glu Asn Val Leu Ile Gly Ile Thr	
65 70 75 80	
Gln Ala Pro Tyr Ile Met Gly Leu Ala Asp Gly Leu Met Lys Asn Asp	
85 90 95	
Ile Pro Tyr Lys Leu Ile Ser Glu Gly Asn Cys Thr Gly Tyr His Leu	
100 105 110	
Pro Ala Lys Gln Thr Ile Thr Leu Ile Glu Gln Asn Gln Leu Trp Arg	
115 120 125	

Asp Ala Phe Tyr Trp Leu Ala Trp Gln Asn Arg Ile Leu Glu Leu Arg  
 130 135 140  
 Asp Val Gln Leu Ile Gly His Asn Ser Tyr Glu Gln Ile Arg Ala Thr  
 145 150 155 160  
 Leu Leu Ser Met Ile Asp Trp Asn Glu Glu Leu Arg Ser Arg Ile Gly  
 165 170 175  
 Val Met Asn Tyr Ile His Gln Arg Thr Arg Ile Ser Arg Ser Val Val  
 180 185 190  
 Ala Glu Val Leu Ala Ala Leu Arg Lys Gly Gly Tyr Ile Glu Met Asn  
 195 200 205  
 Lys Gly Lys Leu Val Ala Ile Asn Arg Leu Pro Ser Glu Tyr  
 210 215 220

<210> 383  
 <211> 84  
 <212> PRT  
 <213> E. Coli

<400> 383  
 Met Thr Asp Lys Ile Arg Thr Leu Gln Gly Arg Val Val Ser Asp Lys  
 1 5 10 15  
 Met Glu Lys Ser Ile Val Val Ala Ile Glu Arg Phe Val Lys His Pro  
 20 25 30  
 Ile Tyr Gly Lys Phe Ile Lys Arg Thr Thr Lys Leu His Val His Asp  
 35 40 45  
 Glu Asn Asn Glu Cys Gly Ile Gly Asp Val Val Glu Ile Arg Glu Cys  
 50 55 60  
 Arg Pro Leu Ser Lys Thr Lys Ser Trp Thr Leu Val Arg Val Val Glu  
 65 70 75 80  
 Lys Ala Val Leu

<210> 384  
 <211> 63  
 <212> PRT  
 <213> E. Coli

<400> 384  
 Met Lys Ala Lys Glu Leu Arg Glu Lys Ser Val Glu Glu Leu Asn Thr  
 1 5 10 15  
 Glu Leu Leu Asn Leu Leu Arg Glu Gln Phe Asn Leu Arg Met Gln Ala  
 20 25 30  
 Ala Ser Gly Gln Leu Gln Gln Ser His Leu Leu Lys Gln Val Arg Arg  
 35 40 45  
 Asp Val Ala Arg Val Lys Thr Leu Leu Asn Glu Lys Ala Gly Ala  
 50 55 60

<210> 385  
 <211> 136  
 <212> PRT  
 <213> E. Coli

<400> 385  
 Met Leu Gln Pro Lys Arg Thr Lys Phe Arg Lys Met His Lys Gly Arg  
 1 5 10 15  
 Asn Arg Gly Leu Ala Gln Gly Thr Asp Val Ser Phe Gly Ser Phe Gly  
 20 25 30  
 Leu Lys Ala Val Gly Arg Gly Arg Leu Thr Ala Arg Gln Ile Glu Ala

35 40 45  
 Ala Arg Arg Ala Met Thr Arg Ala Val Lys Arg Gln Gly Lys Ile Trp  
 50 55 60  
 Ile Arg Val Phe Pro Asp Lys Pro Ile Thr Glu Lys Pro Leu Ala Val  
 65 70 75 80  
 Arg Met Gly Lys Gly Lys Gly Asn Val Glu Tyr Trp Val Ala Leu Ile  
 85 90 95  
 Gln Pro Gly Lys Val Leu Tyr Glu Met Asp Gly Val Pro Glu Glu Leu  
 100 105 110  
 Ala Arg Glu Ala Phe Lys Leu Ala Ala Lys Leu Pro Ile Lys Thr  
 115 120 125  
 Thr Phe Val Thr Lys Thr Val Met  
 130 135

<210> 386  
 <211> 233  
 <212> PRT  
 <213> E. Coli

<400> 386  
 Met Gly Gln Lys Val His Pro Asn Gly Ile Arg Leu Gly Ile Val Lys  
 1 5 10 15  
 Pro Trp Asn Ser Thr Trp Phe Ala Asn Thr Lys Glu Phe Ala Asp Asn  
 20 25 30  
 Leu Asp Ser Asp Phe Lys Val Arg Gln Tyr Leu Thr Lys Glu Leu Ala  
 35 40 45  
 Lys Ala Ser Val Ser Arg Ile Val Ile Glu Arg Pro Ala Lys Ser Ile  
 50 55 60  
 Arg Val Thr Ile His Thr Ala Arg Pro Gly Ile Val Ile Gly Lys Lys  
 65 70 75 80  
 Gly Glu Asp Val Glu Lys Leu Arg Lys Val Val Ala Asp Ile Ala Gly  
 85 90 95  
 Val Pro Ala Gln Ile Asn Ile Ala Glu Val Arg Lys Pro Glu Leu Asp  
 100 105 110  
 Ala Lys Leu Val Ala Asp Ser Ile Thr Ser Gln Leu Glu Arg Arg Val  
 115 120 125  
 Met Phe Arg Arg Ala Met Lys Arg Ala Val Gln Asn Ala Met Arg Leu  
 130 135 140  
 Gly Ala Lys Gly Ile Lys Val Glu Val Ser Gly Arg Leu Gly Gly Ala  
 145 150 155 160  
 Glu Ile Ala Arg Thr Glu Trp Tyr Arg Glu Gly Arg Val Pro Leu His  
 165 170 175  
 Thr Leu Arg Ala Asp Ile Asp Tyr Asn Thr Ser Glu Ala His Thr Thr  
 180 185 190  
 Tyr Gly Val Ile Gly Val Lys Val Trp Ile Phe Lys Gly Glu Ile Leu  
 195 200 205  
 Gly Gly Met Ala Ala Val Glu Gln Pro Glu Lys Pro Ala Ala Gln Pro  
 210 215 220  
 Lys Lys Gln Gln Arg Lys Gly Arg Lys  
 225 230

<210> 387  
 <211> 110  
 <212> PRT  
 <213> E. Coli

<400> 387

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Met Glu Thr Ile Ala Lys His Arg His Ala Arg Ser Ser Ala Gln Lys
 1          5          10          15
Val Arg Leu Val Ala Asp Leu Ile Arg Gly Lys Lys Val Ser Gln Ala
 20          25          30
Leu Asp Ile Leu Thr Tyr Thr Asn Lys Lys Ala Ala Val Leu Val Lys
 35          40          45
Lys Val Leu Glu Ser Ala Ile Ala Asn Ala Glu His Asn Asp Gly Ala
 50          55          60
Asp Ile Asp Asp Leu Lys Val Thr Lys Ile Phe Val Asp Glu Gly Pro
 65          70          75          80
Ser Met Lys Arg Ile Met Pro Arg Ala Lys Gly Arg Ala Asp Arg Ile
 85          90          95
Leu Lys Arg Thr Ser His Ile Thr Val Val Val Ser Asp Arg
 100          105          110

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<210> 388  
 <211> 92  
 <212> PRT  
 <213> E. Coli

```

<400> 388
Met Pro Arg Ser Leu Lys Lys Gly Pro Phe Ile Asp Leu His Leu Leu
 1          5          10          15
Met Lys Val Glu Lys Ala Val Glu Ser Gly Asp Lys Lys Pro Leu Arg
 20          25          30
Thr Trp Ser Arg Arg Ser Thr Ile Phe Pro Asn Met Ile Gly Leu Thr
 35          40          45
Ile Ala Val His Asn Gly Arg Gln His Val Pro Val Phe Val Thr Asp
 50          55          60
Glu Met Val Gly His Lys Leu Gly Glu Phe Ala Pro Thr Arg Thr Tyr
 65          70          75          80
Arg Gly His Ala Ala Asp Lys Lys Ala Lys Lys Lys
 85          90

```

<210> 389  
 <211> 273  
 <212> PRT  
 <213> E. Coli

```

<400> 389
Met Ala Val Val Lys Cys Lys Pro Thr Ser Pro Gly Arg Arg His Val
 1          5          10          15
Val Lys Val Val Asn Pro Glu Leu His Lys Gly Lys Pro Phe Ala Pro
 20          25          30
Leu Leu Glu Lys Asn Ser Lys Ser Gly Gly Arg Asn Asn Gly Arg
 35          40          45
Ile Thr Thr Arg His Ile Gly Gly Gly His Lys Gln Ala Tyr Arg Ile
 50          55          60
Val Asp Phe Lys Arg Asn Lys Asp Gly Ile Pro Ala Val Val Glu Arg
 65          70          75          80
Leu Glu Tyr Asp Pro Asn Arg Ser Ala Asn Ile Ala Leu Val Leu Tyr
 85          90          95
Lys Asp Gly Glu Arg Arg Tyr Ile Leu Ala Pro Lys Gly Leu Lys Ala
 100          105          110
Gly Asp Gln Ile Gln Ser Gly Val Asp Ala Ala Ile Lys Pro Gly Asn
 115          120          125
Thr Leu Pro Met Arg Asn Ile Pro Val Gly Ser Thr Val His Asn Val

```

130 135 140  
 Glu Met Lys Pro Gly Lys Gly Gly Gln Leu Ala Arg Ser Ala Gly Thr  
 145 150 155 160  
 Tyr Val Gln Ile Val Ala Arg Asp Gly Ala Tyr Val Thr Leu Arg Leu  
 165 170 175  
 Arg Ser Gly Glu Met Arg Lys Val Glu Ala Asp Cys Arg Ala Thr Leu  
 180 185 190  
 Gly Glu Val Gly Asn Ala Glu His Met Leu Arg Val Leu Gly Lys Ala  
 195 200 205  
 Gly Ala Ala Arg Trp Arg Gly Val Arg Pro Thr Val Arg Gly Thr Ala  
 210 215 220  
 Met Asn Pro Val Asp His Pro His Gly Gly Gly Glu Gly Arg Asn Phe  
 225 230 235 240  
 Gly Lys His Pro Val Thr Pro Trp Gly Val Gln Thr Lys Gly Lys Lys  
 245 250 255  
 Thr Arg Ser Asn Lys Arg Thr Asp Lys Phe Ile Val Arg Arg Arg Ser  
 260 265 270  
 Lys

<210> 390  
 <211> 100  
 <212> PRT  
 <213> E. Coli

<400> 390  
 Met Ile Arg Glu Glu Arg Leu Leu Lys Val Leu Arg Ala Pro His Val  
 1 5 10 15  
 Ser Glu Lys Ala Ser Thr Ala Met Glu Lys Ser Asn Thr Ile Val Leu  
 20 25 30  
 Lys Val Ala Lys Asp Ala Thr Lys Ala Glu Ile Lys Ala Ala Val Gln  
 35 40 45  
 Lys Leu Phe Glu Val Glu Val Glu Val Val Asn Thr Leu Val Val Lys  
 50 55 60  
 Gly Lys Val Lys Arg His Gly Gln Arg Ile Gly Arg Arg Ser Asp Trp  
 65 70 75 80  
 Lys Lys Ala Tyr Val Thr Leu Lys Glu Gly Gln Asn Leu Asp Phe Val  
 85 90 95  
 Gly Gly Ala Glu  
 100

<210> 391  
 <211> 201  
 <212> PRT  
 <213> E. Coli

<400> 391  
 Met Glu Leu Val Leu Lys Asp Ala Gln Ser Ala Leu Thr Val Ser Glu  
 1 5 10 15  
 Thr Thr Phe Gly Arg Asp Phe Asn Glu Ala Leu Val His Gln Val Val  
 20 25 30  
 Val Ala Tyr Ala Ala Gly Ala Arg Gln Gly Thr Arg Ala Gln Lys Thr  
 35 40 45  
 Arg Ala Glu Val Thr Gly Ser Gly Lys Lys Pro Trp Arg Gln Lys Gly  
 50 55 60  
 Thr Gly Arg Ala Arg Ser Gly Ser Ile Lys Ser Pro Ile Trp Arg Ser  
 65 70 75 80

Gly Gly Val Thr Phe Ala Ala Arg Pro Gln Asp His Ser Gln Lys Val  
 85 90 95  
 Asn Lys Lys Met Tyr Arg Gly Ala Leu Lys Ser Ile Leu Ser Glu Leu  
 100 105 110  
 Val Arg Gln Asp Arg Leu Ile Val Val Glu Lys Phe Ser Val Glu Ala  
 115 120 125  
 Pro Lys Thr Lys Leu Leu Ala Gln Lys Leu Lys Asp Met Ala Leu Glu  
 130 135 140  
 Asp Val Leu Ile Ile Thr Gly Glu Leu Asp Glu Asn Leu Phe Leu Ala  
 145 150 155 160  
 Ala Arg Asn Leu His Lys Val Asp Val Arg Asp Ala Thr Gly Ile Asp  
 165 170 175  
 Pro Val Ser Leu Ile Ala Phe Asp Lys Val Val Met Thr Ala Asp Ala  
 180 185 190  
 Val Lys Gln Val Glu Glu Met Leu Ala  
 195 200

<210> 392  
 <211> 209  
 <212> PRT  
 <213> E. Coli

<400> 392  
 Met Ile Gly Leu Val Gly Lys Lys Val Gly Met Thr Arg Ile Phe Thr  
 1 5 10 15  
 Glu Asp Gly Val Ser Ile Pro Val Thr Val Ile Glu Val Glu Ala Asn  
 20 25 30  
 Arg Val Thr Gln Val Lys Asp Leu Ala Asn Asp Gly Tyr Arg Ala Ile  
 35 40 45  
 Gln Val Thr Thr Gly Ala Lys Lys Ala Asn Arg Val Thr Lys Pro Glu  
 50 55 60  
 Ala Gly His Phe Ala Lys Ala Gly Val Glu Ala Gly Arg Gly Leu Trp  
 65 70 75 80  
 Glu Phe Arg Leu Ala Glu Gly Glu Glu Phe Thr Val Gly Gln Ser Ile  
 85 90 95  
 Ser Val Glu Leu Phe Ala Asp Val Lys Lys Val Asp Val Thr Gly Thr  
 100 105 110  
 Ser Lys Gly Lys Gly Phe Ala Gly Thr Val Lys Arg Trp Asn Phe Arg  
 115 120 125  
 Thr Gln Asp Ala Thr His Gly Asn Ser Leu Ser His Arg Val Pro Gly  
 130 135 140  
 Ser Ile Gly Gln Asn Gln Thr Pro Gly Lys Val Phe Lys Gly Lys Lys  
 145 150 155 160  
 Met Ala Gly Gln Met Gly Asn Glu Arg Val Thr Val Gln Ser Leu Asp  
 165 170 175  
 Val Val Arg Val Asp Ala Glu Arg Asn Leu Leu Leu Val Lys Gly Ala  
 180 185 190  
 Val Pro Gly Ala Thr Gly Ser Asp Leu Ile Val Lys Pro Ala Val Lys  
 195 200 205  
 Ala

<210> 393  
 <211> 103  
 <212> PRT  
 <213> E. Coli



&lt;400&gt; 393

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Met Gln Asn Gln Arg Ile Arg Ile Arg Leu Lys Ala Phe Asp His Arg
 1          5          10          15
Leu Ile Asp Gln Ala Thr Ala Glu Ile Val Glu Thr Ala Lys Arg Thr
          20          25          30
Gly Ala Gln Val Arg Gly Pro Ile Pro Leu Pro Thr Arg Lys Glu Arg
          35          40          45
Phe Thr Val Leu Ile Ser Pro His Val Asn Lys Asp Ala Arg Asp Gln
          50          55          60
Tyr Glu Ile Arg Thr His Leu Arg Leu Val Asp Ile Val Glu Pro Thr
65          70          75          80
Glu Lys Thr Val Asp Ala Leu Met Arg Leu Asp Leu Ala Ala Gly Val
          85          90          95
Asp Val Gln Ile Ser Leu Gly
          100

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&lt;210&gt; 394

&lt;211&gt; 118

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 394

```

Met Ala Arg Val Lys Arg Gly Val Ile Ala Arg Ala Arg His Lys Lys
 1          5          10          15
Ile Leu Lys Gln Ala Lys Gly Tyr Tyr Gly Ala Arg Ser Arg Val Tyr
          20          25          30
Arg Val Ala Phe Gln Ala Val Ile Lys Ala Gly Gln Tyr Ala Tyr Arg
          35          40          45
Asp Arg Arg Gln Arg Lys Arg Gln Phe Arg Gln Leu Trp Ile Ala Arg
          50          55          60
Ile Asn Ala Ala Ala Arg Gln Asn Gly Ile Ser Tyr Ser Lys Phe Ile
65          70          75          80
Asn Gly Leu Lys Lys Ala Ser Val Glu Ile Asp Arg Lys Ile Leu Ala
          85          90          95
Asp Ile Ala Val Phe Asp Lys Val Ala Phe Thr Ala Leu Val Glu Lys
          100          105          110
Ala Lys Ala Ala Leu Ala
          115

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&lt;210&gt; 395

&lt;211&gt; 65

&lt;212&gt; PRT

&lt;213&gt; E. Coli

&lt;400&gt; 395

```

Met Pro Lys Ile Lys Thr Val Arg Gly Ala Ala Lys Arg Phe Lys Lys
 1          5          10          15
Thr Gly Lys Gly Gly Phe Lys His Lys His Ala Asn Leu Arg His Ile
          20          25          30
Leu Thr Lys Lys Ala Thr Lys Arg Lys Arg His Leu Arg Pro Lys Ala
          35          40          45
Met Val Ser Lys Gly Asp Leu Gly Leu Val Ile Ala Cys Leu Pro Tyr
50          55          60
Ala
65

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<210> 396  
 <211> 180  
 <212> PRT  
 <213> E. Coli

<400> 396  
 Met Lys Gly Gly Lys Arg Val Gln Thr Ala Arg Pro Asn Arg Ile Asn  
 1 5 10 15  
 Gly Glu Ile Arg Ala Gln Glu Val Arg Leu Thr Gly Leu Glu Gly Glu  
 20 25 30  
 Gln Leu Gly Ile Val Ser Leu Arg Glu Ala Leu Glu Lys Ala Glu Glu  
 35 40 45  
 Ala Gly Val Asp Leu Val Glu Ile Ser Pro Asn Ala Glu Pro Pro Val  
 50 55 60  
 Cys Arg Ile Met Asp Tyr Gly Lys Phe Leu Tyr Glu Lys Ser Lys Ser  
 65 70 75 80  
 Ser Lys Glu Gln Lys Lys Lys Gln Lys Val Ile Gln Val Lys Glu Ile  
 85 90 95  
 Lys Phe Arg Pro Gly Thr Asp Glu Gly Asp Tyr Gln Val Lys Leu Arg  
 100 105 110  
 Ser Leu Ile Arg Phe Leu Glu Glu Gly Asp Lys Ala Lys Ile Thr Leu  
 115 120 125  
 Arg Phe Arg Gly Arg Glu Met Ala His Gln Gln Ile Gly Met Glu Val  
 130 135 140  
 Leu Asn Arg Val Lys Asp Asp Leu Gln Glu Leu Ala Val Val Glu Ser  
 145 150 155 160  
 Phe Pro Thr Lys Ile Glu Gly Arg Gln Met Ile Met Val Leu Ala Pro  
 165 170 175  
 Lys Lys Lys Gln  
 180

<210> 397  
 <211> 642  
 <212> PRT  
 <213> E. Coli

<400> 397  
 Met Pro Val Ile Thr Leu Pro Asp Gly Ser Gln Arg His Tyr Asp His  
 1 5 10 15  
 Ala Val Ser Pro Met Asp Val Ala Leu Asp Ile Gly Pro Gly Leu Ala  
 20 25 30  
 Lys Ala Cys Ile Ala Gly Arg Val Asn Gly Glu Leu Val Asp Ala Cys  
 35 40 45  
 Asp Leu Ile Glu Asn Asp Ala Gln Leu Ser Ile Ile Thr Ala Lys Asp  
 50 55 60  
 Glu Glu Gly Leu Glu Ile Ile Arg His Ser Cys Ala His Leu Leu Gly  
 65 70 75 80  
 His Ala Ile Lys Gln Leu Trp Pro His Thr Lys Met Ala Ile Gly Pro  
 85 90 95  
 Val Ile Asp Asn Gly Phe Tyr Tyr Asp Val Asp Leu Asp Arg Thr Leu  
 100 105 110  
 Thr Gln Glu Asp Val Glu Ala Leu Glu Lys Arg Met His Glu Leu Ala  
 115 120 125  
 Glu Lys Asn Tyr Asp Val Ile Lys Lys Lys Val Ser Trp His Glu Ala  
 130 135 140  
 Arg Glu Thr Phe Ala Asn Arg Gly Glu Ser Tyr Lys Val Ser Ile Leu  
 145 150 155 160  
 Asp Glu Asn Ile Ala His Asp Asp Lys Pro Gly Leu Tyr Phe His Glu  
 165 170 175

Glu Tyr Val Asp Met Cys Arg Gly Pro His Val Pro Asn Met Arg Phe  
 180 185 190  
 Cys His His Phe Lys Leu Met Lys Thr Ala Gly Ala Tyr Trp Arg Gly  
 195 200 205  
 Asp Ser Asn Asn Lys Met Leu Gln Arg Ile Tyr Gly Thr Ala Trp Ala  
 210 215 220  
 Asp Lys Lys Ala Leu Asn Ala Tyr Leu Gln Arg Leu Glu Glu Ala Ala  
 225 230 235 240  
 Lys Arg Asp His Arg Lys Ile Gly Lys Gln Leu Asp Leu Tyr His Met  
 245 250 255  
 Gln Glu Glu Ala Pro Gly Met Val Phe Trp His Asn Asp Gly Trp Thr  
 260 265 270  
 Ile Phe Arg Glu Leu Glu Val Phe Val Arg Ser Lys Leu Lys Glu Tyr  
 275 280 285  
 Gln Tyr Gln Glu Val Lys Gly Pro Phe Met Met Asp Arg Val Leu Trp  
 290 295 300  
 Glu Lys Thr Gly His Trp Asp Asn Tyr Lys Asp Ala Met Phe Thr Thr  
 305 310 315 320  
 Ser Ser Glu Asn Arg Glu Tyr Cys Ile Lys Pro Met Asn Cys Pro Gly  
 325 330 335  
 His Val Gln Ile Phe Asn Gln Gly Leu Lys Ser Tyr Arg Asp Leu Pro  
 340 345 350  
 Leu Arg Met Ala Glu Phe Gly Ser Cys His Arg Asn Glu Pro Ser Gly  
 355 360 365  
 Ser Leu His Gly Leu Met Arg Val Arg Gly Phe Thr Gln Asp Asp Ala  
 370 375 380  
 His Ile Phe Cys Thr Glu Glu Gln Ile Arg Asp Glu Val Asn Gly Cys  
 385 390 395 400  
 Ile Arg Leu Val Tyr Asp Met Tyr Ser Thr Phe Gly Phe Glu Lys Ile  
 405 410 415  
 Val Val Lys Leu Ser Thr Arg Pro Glu Lys Arg Ile Gly Ser Asp Glu  
 420 425 430  
 Met Trp Asp Arg Ala Glu Ala Asp Leu Ala Val Ala Leu Glu Glu Asn  
 435 440 445  
 Asn Ile Pro Phe Glu Tyr Gln Leu Gly Glu Gly Ala Phe Tyr Gly Pro  
 450 455 460  
 Lys Ile Glu Phe Thr Leu Tyr Asp Cys Leu Asp Arg Ala Trp Gln Cys  
 465 470 475 480  
 Gly Thr Val Gln Leu Asp Phe Ser Leu Pro Ser Arg Leu Ser Ala Ser  
 485 490 495  
 Tyr Val Gly Glu Asp Asn Glu Arg Lys Val Pro Val Met Ile His Arg  
 500 505 510  
 Ala Ile Leu Gly Ser Met Glu Arg Phe Ile Gly Ile Leu Thr Glu Glu  
 515 520 525  
 Phe Ala Gly Phe Phe Pro Thr Trp Leu Ala Pro Val Gln Val Val Ile  
 530 535 540  
 Met Asn Ile Thr Asp Ser Gln Ser Glu Tyr Val Asn Glu Leu Thr Gln  
 545 550 555 560  
 Lys Leu Ser Asn Ala Gly Ile Arg Val Lys Ala Asp Leu Arg Asn Glu  
 565 570 575  
 Lys Ile Gly Phe Lys Ile Arg Glu His Thr Leu Arg Arg Val Pro Tyr  
 580 585 590  
 Met Leu Val Cys Gly Asp Lys Glu Val Glu Ser Gly Lys Val Ala Val  
 595 600 605  
 Arg Thr Arg Arg Gly Lys Asp Leu Gly Ser Met Asp Val Asn Glu Val  
 610 615 620  
 Ile Glu Lys Leu Gln Gln Glu Ile Arg Ser Arg Ser Leu Lys Gln Leu  
 625 630 635 640  
 Glu Glu

<210> 398  
 <211> 450  
 <212> PRT  
 <213> E. Coli

<400> 398

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Met Thr Lys His Tyr Asp Tyr Ile Ala Ile Gly Gly Gly Ser Gly Gly
 1          5          10          15
Ile Ala Ser Ile Asn Arg Ala Ala Met Tyr Gly Gln Lys Cys Ala Leu
          20          25          30
Ile Glu Ala Lys Glu Leu Gly Gly Thr Cys Val Asn Val Gly Cys Val
          35          40          45
Pro Lys Lys Val Met Trp His Ala Ala Gln Ile Arg Glu Ala Ile His
          50          55          60
Met Tyr Gly Pro Asp Tyr Gly Phe Asp Thr Thr Ile Asn Lys Phe Asn
          65          70          75          80
Trp Glu Thr Leu Ile Ala Ser Arg Thr Ala Tyr Ile Asp Arg Ile His
          85          90          95
Thr Ser Tyr Glu Asn Val Leu Gly Lys Asn Asn Val Asp Val Ile Lys
          100          105          110
Gly Phe Ala Arg Phe Val Asp Ala Lys Thr Leu Glu Val Asn Gly Glu
          115          120          125
Thr Ile Thr Ala Asp His Ile Leu Ile Ala Thr Gly Gly Arg Pro Ser
          130          135          140
His Pro Asp Ile Pro Gly Val Glu Tyr Gly Ile Asp Ser Asp Gly Phe
          145          150          155          160
Phe Ala Leu Pro Ala Leu Pro Glu Arg Val Ala Val Val Gly Ala Gly
          165          170          175
Tyr Ile Ala Val Glu Leu Ala Gly Val Ile Asn Gly Leu Gly Ala Lys
          180          185          190
Thr His Leu Phe Val Arg Lys His Ala Pro Leu Arg Ser Phe Asp Pro
          195          200          205
Met Ile Ser Glu Thr Leu Val Glu Val Met Asn Ala Glu Gly Pro Gln
          210          215          220
Leu His Thr Asn Ala Ile Pro Lys Ala Val Val Lys Asn Thr Asp Gly
          225          230          235          240
Ser Leu Thr Leu Glu Leu Glu Asp Gly Arg Ser Glu Thr Val Asp Cys
          245          250          255
Leu Ile Trp Ala Ile Gly Arg Glu Pro Ala Asn Asp Asn Ile Asn Leu
          260          265          270
Glu Ala Ala Gly Val Lys Thr Asn Glu Lys Gly Tyr Ile Val Val Asp
          275          280          285
Lys Tyr Gln Asn Thr Asn Ile Glu Gly Ile Tyr Ala Val Gly Asp Asn
          290          295          300
Thr Gly Ala Val Glu Leu Thr Pro Val Ala Val Ala Ala Gly Arg Arg
          305          310          315          320
Leu Ser Glu Arg Leu Phe Asn Asn Lys Pro Asp Glu His Leu Asp Tyr
          325          330          335
Ser Asn Ile Pro Thr Val Val Phe Ser His Pro Pro Ile Gly Thr Val
          340          345          350
Gly Leu Thr Glu Pro Gln Ala Arg Glu Gln Tyr Gly Asp Asp Gln Val
          355          360          365
Lys Val Tyr Lys Ser Ser Phe Thr Ala Met Tyr Thr Ala Val Thr Thr
          370          375          380
His Arg Gln Pro Cys Arg Met Lys Leu Val Cys Val Gly Ser Glu Glu
          385          390          395          400
Lys Ile Val Gly Ile His Gly Ile Gly Phe Gly Met Asp Glu Met Leu
          405          410          415
Gln Gly Phe Ala Val Ala Leu Lys Met Gly Ala Thr Lys Lys Asp Phe
          420          425          430

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Asp Asn Thr Val Ala Ile His Pro Thr Ala Ala Glu Glu Phe Val Thr  
 435 440 445  
 Met Arg  
 450

<210> 399  
 <211> 2894  
 <212> RNA  
 <213> E. Coli

<400> 399

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cccggccuau	caacgucguc	gucuuaacg	uuccuucagg	accuuuaaag	ggucaggagg	120
aacucaucuc	ggggcaaguu	ucgugcuuag	augcuuucag	cacuuauucuc	uuccgcauuu	180
agcuaccggg	cagugccaau	ggcaugacaa	cccgaacacc	agugaugcgu	ccacuccggu	240
ccucucguac	uaggagcagc	ccccucagu	ucuccagcgc	ccacggcaga	uagggaccga	300
acugucucac	gacguucuaa	acccagcucg	cguaccacuu	uaaauggcga	acagccauac	360
ccuuggggacc	uacuucagcc	ccaggaugug	augagccgac	aucgaggugc	caaacaccgc	420
cgucgauaug	aacucuuggg	cgguaucagc	cuguuaucac	cggaguaccu	uuuauccggu	480
gagcgauagg	ccuuccauuc	agaaccaccg	gaucacuaug	accugcuuuc	gcaccugcuc	540
gcgcgcgucac	gcucgcgaguc	aagcuggcgu	augccauuug	acuaaccucc	ugauguccga	600
ccaggauuag	ccaaccuucg	ugcuccuccg	uuacucuuaa	ggaggagacc	gccccaguca	660
aacuaccac	cagacacugu	ccgcaaccgc	gauuacgggu	caacguuaga	acaucaaaaca	720
uuaaagggug	guauuucag	gucggcucca	ugcagacugg	cguccacacu	ucaaagccuc	780
ccaccuaucc	uacacaucaa	ggcucaaugu	ucagugucua	gcuaauagua	agguuacagg	840
ggucuauuccg	ucugccgcg	gguacacugc	aucuucacag	cgaguucuuu	uucacugagu	900
ccggggugga	gacagccugg	ccaucuuuac	gccauucgug	caggucggaa	cuuaccgcgac	960
aaggaaauuc	gcuaccuuag	gaccguuaua	guuacggcgc	ccguuuaccg	gggcuucgau	1020
caagagcuuc	gcuugcgcuu	accccaucaa	uuuaccuucc	ggcaccgggc	aggcgucaca	1080
ccguauacgu	ccacuucggu	guuugcacag	ugcuguguuu	uuauuaaaca	guugcagcca	1140
gcugguauuc	ucgacugauu	ucagcuccau	ccgcgaggga	ccuaccuac	auaucagcgu	1200
gccuucuccc	gaaguuacgg	caccauuuug	ccuaguuccu	ucacccgagu	ucucucaagc	1260
gccuugguau	ucucuaccug	accaccugug	ucgguuuggg	guacgauuug	auguuaccug	1320
augcuuagag	gcuuuuccug	gaagcagggc	auuuguugcu	ucagcaccgu	agugccucgu	1380
caucacgccu	cagccuugau	uuuccggauu	ugccuggaaa	accagccuac	acgcuuaaac	1440
cgggacaacc	gucgcccggc	caacauagcc	uucuccgucg	ccccuucgca	guaacaccaa	1500
guacaggaau	auuaaccugu	uucccaucga	cuacgccuuu	cggccucgcc	uuaggggucg	1560
acucaccucg	ccccgauuaa	cguuggacag	gaaccuuugg	ucuuuccggc	agcgggcuuu	1620
ucaccgcguu	uauuguuacu	uauugcagca	uucgcacuuu	ugauaccucc	agcaugccuc	1680
acagcacacc	uucgcaggcu	uacagaacgc	uccccuacc	aacaacgcau	aagcgucgcu	1740
gccgcagcuu	cggugcaugg	uuuagccccg	uuacaucuuu	cgcgcaggcc	gacucgacca	1800
gugagcuauu	acgcuuucuu	uaaaugaugg	cugcuucuaa	gccaacauc	uggcugucug	1860
ggccuuccca	caucguuucc	cacuuuaacca	ugacuugggg	accuuagcug	gcggucuggg	1920
uuguuuuccu	cuucacgacg	gacguuagca	ccgcgcgugu	gucucccgug	auaacaauuc	1980
ccgguaucg	caguugcau	cggguuggua	acuggggaug	acccccuugc	cgaaacagug	2040
cucuaccccc	ggagaugaau	ucacgaggcg	cuaccuaaa	agcuuucggg	gagaaccagc	2100
uauuccccgg	uuugauuggc	cuuucacccc	cagccacaag	ucauccgcua	auuuuuaaac	2160
auuagucggg	ucgguccucc	aguuaguguu	acccaaccuu	caaccugccc	auggcuaagau	2220
caccggguuu	cgggucuaau	cccugcaacu	uaacgcccag	uuagacucg	guuucccuuc	2280
ggcuccccua	uucgguaaac	cuugcuacag	aaauuaaguc	gcugacccau	uauacaaaag	2340
guacgcaguc	acacgccuaa	gcgugcuccc	acugcuugua	cguacacggg	uucagguucu	2400
uuuucacucc	ccucgcgggg	guuucuuuuc	ccuuucccuc	acgguacugg	uucacuaucg	2460
gucagucagg	aguauuuagc	cuuggaggau	ggucccccca	uaauacagac	ggauaccacg	2520
ugucccgccc	uacucaucga	gcucacagca	ugugcauuuu	uguguacggg	gcucgacccc	2580
uguaucgcg	gccuuuccag	acgcuuccac	uaacacacac	acugauucag	gcucugggcu	2640
gcuccccguu	cgcucgccc	uacuggggga	aucucggguu	auuucuuuuc	cucggggua	2700
uuagauguuu	caguuccccc	gguucgccuc	auuaaccuau	ggauucaguu	aaugauagug	2760
ugucgaaaca	cacuggguuu	ccccauucgg	aaaucgccc	uuauaacggg	ucauauacc	2820
uuaccgacgc	uuauccgaga	uuagcacguc	cuuauccg	ucugacugcc	agggcaucca	2880

ccguguacgc uuagucgcuu aacc

2894

<210> 400  
 <211> 120  
 <212> RNA  
 <213> E. Coli

&lt;400&gt; 400

augccuggca guucccuacu cucgcauggg gagacccac acuaccaucg gcgcuacggc 60  
 guuucacuuc ugaguucggc auggggucag gugggaccac cgcgcuacgg ccgccaaggca 120

<210> 401  
 <211> 76  
 <212> RNA  
 <213> E. Coli

&lt;400&gt; 401

gucccccucg ucuagaggcc caggacaccg cccuuucacg gcgguaacag gggguucgaau 60  
 cccuagggg acgcca 76

<210> 402  
 <211> 1549  
 <212> RNA  
 <213> E. Coli

&lt;400&gt; 402

aaauugaaga guuugaucu ggcucagauu gaacgcuggc ggcaggccua acacaugcaa 60  
 gucgaacggu aacaggaagc agcuugcugc uucgcugacg aguggcggac gggugaguaa 120  
 ugucugggaa gcugccugau ggagggggau aacuacugga aacgguagcu aaauaccgcau 180  
 aaugucgcaa gaccaaagag ggggaccuuc gggccucuuu ccaucggauug ugcccagauug 240  
 ggauuagcuu guuggugggg uaacggcuca ccaaggcgac gaucuuuagc uggucugaga 300  
 ggaugaccag ccacacugga acugagacac gguccagacu ccuacgggag gcagcagugg 360  
 ggaauauugc acaauugggc caagccugau gcagccaugc cgcguguaug aagaaggccu 420  
 ucggguugua aaguacuuuc agcggggagg aaggaguaa aguuauuacc uuugcucauu 480  
 gacguuaccc gcagaagaag caccggcuua cuccgugcca gcagccgagg uauuacggag 540  
 ggugcaagcg uuaauccgga uuacugggcg uaaagcgac gcaggcgggu ugguuuaguc 600  
 agaugugaaa uccccgggcu caaccuggga acugcaucug auacuggcaa gcuugagucu 660  
 cguagagggg gguagaauuc cagguguagc ggugaaaugc guagagauuc ggaggaauac 720  
 cggugggcgaa ggcggcccc uggacgaaga cugacgcuca ggugcgaaag cguggggagc 780  
 aaacaggauu agauaccug guaguccacg ccguaaacga ugucgacuug gagguugugc 840  
 ccuugaggcg uggcuuccgg agcuuacggc uuaagucgac cgcugggga guacggccgc 900  
 aagguuauaa cucaauugaa uugacggggg cccgcacaag cgguggagca ugugguuuaa 960  
 uucgaugcaa cgcgaagaac cuuaccuggu cuugacauc acggaaguuu ucagagauga 1020  
 gaauugccu ucgggaaccg ugagacaggu gcugcauggc ugucgucagc ucguuugug 1080  
 aaauugggg uuaagucccg caacgagcgc aaccuuuau cuuuguuugc agcgguccgg 1140  
 ccgggaacuc aaaggagacu gccagugaua aacuggagga agguaggga gacgucaagu 1200  
 caucauggcc cuuacgacca gggcuacaca cgugcuacaa uggcgcauac aaagagaagc 1260  
 gaccucgcga gagcaagcgg accucauaaa gugcgucgua guccggauug gagucugcaa 1320  
 cucgacucca ugaagucgga aucgcuagua aucguggauc agaaugccac ggugaauacg 1380  
 uucccgggcc uuguacacac cgcggcugac accaugggag uggguugcaa aagaaguagg 1440  
 uagcuuaacc uucgggaggg cgcuuaccac uuugugauuc augacugggg ugaagucgua 1500  
 acaagguaac cguaggggaa ccugcgguug gaucaccucc uuaccuuuaa 1549

<210> 403  
 <211> 17  
 <212> DNA  
 <213> Artificial  
 <220>  
 <223> Primer Oligonucleotide

<400> 403  
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17

<210> 404  
 <211> 18  
 <212> DNA  
 <213> Artificial  
 <220>  
 <223> Primer Oligonucleotide

<400> 404  
 acaatttcac acagcctc

18

<210> 405  
 <211> 159  
 <212> DNA  
 <213> Escherichia coli

<400> 405  
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 atcaccagca gatgaaataa cgataaccag aacaacgcct tatagcgttg agtttgcgag  
 aaaacgttca tattgtacct ttttgattaa ccattgggg

60  
 120  
 159

<210> 406  
 <211> 640  
 <212> DNA  
 <213> Escherichia coli

<220>  
 <221> misc\_feature  
 <222> (1)...(640)  
 <223> n = A,T,C or G

<400> 406  
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 aanaaaaggc ggggatttgt nagccacggg ngattanttt anaataaatt aagtgttgcc 120  
 ataaggggac aaagngaagg aagtggntat taanggannc gccaatgcga nttagggcag 180  
 accattcggc cattcgctt cttggttatc gaagttcatc cagatagccg ttgccngacc 240  
 gaccagattc gcttcnggca caaagcccca gtaacggctg tccgcgctgt tgcgcggtt 300  
 gtcgccccatc atgaagtatt gtcccggagg aacaatccag gttgccagtt gttgccctgg 360  
 ctgctggtaa tacatcccca cctgacctg cgcaatcggc actgtcagaa tgcggtgcgt 420  
 cacatcaccc agtgtctctt tacgtcggga aagacgaatt ccattttctt tggtttcggt 480  
 tttcggcaact tcaaagaatc cgctggctgc ttcccacca ttacggcgtg agaaggtctg 540  
 aacgaaatcg ctcggttcca cgtttgagta ggtgaccggc agcgcgtttt cacacgcctg 600  
 gccggaactg catcccgggtt gaatcgctcag ctctttttag 640

<210> 407  
 <211> 682  
 <212> DNA  
 <213> Escherichia coli

<220>  
 <221> misc\_feature

&lt;222&gt; (1)...(682)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 407

cctgcagggt	aatgtcgcca	ttaaaactggc	gcaggcagcc	aaagagttgc	tccgcttcta	60
cccagtcggc	agcgacaact	tgcgtttaaag	tcgcaaaatt	atcatctgca	ctcaactgct	120
gacgtaagcg	gatggagtgg	ccggaaacct	catagtgaac	gccaccagt	tggcctgcat	180
cgctttgtag	cgtagcgcg	gcattggcaa	taagattcag	atactcagac	tcttccgggg	240
ccttcgccag	cataaaagag	gaggatgctc	gcgtatgcag	caactgctcc	agcgcaaaatt	300
gcagccgcgg	ttgagtatca	ctgaataaag	gatcgttttc	gtcaatcaaa	tgtggctgag	360
caaataatttc	ctgatagcta	tcggtatcag	gaaccaggtc	acgccatgca	agtttcgtaa	420
tgggtcaaagt	tgatgttttt	tagtctgttg	tcaaagccgc	nattataccn	gtaaccggca	480
ctacagcaca	cgtagaaaagc	acccgacaat	actcctggca	tgggcgttaa	agctcacagg	540
atggagatct	tttcttcact	ggcctaaaaa	gctgatattc	tgtaaagagt	tacacngtaa	600
cattgagatc	gctatgaaat	atcaacaact	tggaaaatct	tgnaaagcng	gttggaaaat	660
ggaaaagtatc	tggttaagaa	gc				682

&lt;210&gt; 408

&lt;211&gt; 309

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 408

ggggatccgg	cagaatttta	cgctgaccaa	tgacgcgacg	acgtggcatg	gaaataactcc	60
gttggttaatt	caggattgtc	caaaactcta	cgagtttagt	ttgacattta	agttaaaacg	120
tttggcctta	cttaacggag	aaccattaag	ccttaggacg	cttcacgcca	tacttggaac	180
gagcctgctt	acggtcttta	acgccggagc	agtcaagcgc	accacgtacg	gtgtggtaac	240
gaacacccgg	gaggtcttta	acacgaccgc	cacggatcag	gatcacggag	tgctcctgca	300
gccaaagctt						309

&lt;210&gt; 409

&lt;211&gt; 1167

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 409

gtcgacccat	ctgtccattg	agcggacagt	ttgtgcaaca	ctattttggt	gaccggaaaa	60
tggaacactt	tccgcaatgc	ctgttgctat	cacgcttaaa	ccatttcatt	gcgatttaca	120
cagaacggac	gtcctgtcgc	agtatattaa	gtcgctgata	gaaacaagca	ttgaaaggca	180
cagcagtagt	caaacagtg	gaaacgctac	tggcgcccta	cagcgcaaaa	aggctgggtga	240
ctaaaaagtc	accagccatc	agcctgattt	ctcaggctgc	aaccggaagg	gttggcttat	300
ttaacttcaa	cttcagcgcc	agcttcttcc	agagcttttt	tcagtgcctc	tgcgtcgtct	360
ttgctcacgc	cttctttcag	agcagccggt	gcagattcta	ccaggctctt	agcttctttc	420
agaccagggc	cagttgcgcc	acgtactgct	ttgataacag	caactttggt	agcgccagca	480
gcttttcagaa	ttacgtcgaa	ttcagttttt	tcttcagcag	cttcaaccgg	gccagcagct	540
acagctacag	cagcagcagc	ggaaacaccg	aatttttctt	ycattgcaga	gatcaagttc	600
tacaacgtcc	attacagaca	tagctgcaac	tgcttcaatg	awttgatctt	tagtgataga	660
catttaaatk	gttcctgaat	atcagaataa	gtttatacgt	aagcgaatgc	gttaaaaaga	720
taactgcgaw	taagcagctt	ytttcgcate	gcgtacagma	gccagagtac	gaaccagttt	780
gccagccgaa	gcttctttca	tggttgccat	caggcgtgca	attgcttctt	cgtaggtcgg	840
cagagttgcc	aggcggtcga	tctgagacgc	cgggatcagc	tcaccttcaa	aggcagcggc	900
tttgacctca	aattttgcat	tcgctttcgc	gaactctttg	aacagacgag	cagcagcgcc	960
cgggtgttcc	atagagtatg	caatcagggt	cggaccaaca	aacgcgtctt	tcaggcactc	1020
gaacggagta	ccttcaacag	cacggcgcag	cagggtgtta	cgaacaacac	gcatgtatac	1080
gccagcttcg	cgacctgctt	tacgcagttc	agtcatttta	tctacagtta	cgccacggg	1140
aatccgcaac	tactgcaagc	caagctt				1167

&lt;210&gt; 410

&lt;211&gt; 404

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli



<400> 410  
 caacmctatt ttgktggacc ggaaaakgga acactttccg cawkgcctgt tgctatcacg 60  
 cttaaaccat ttcatcgcga ttacacaga acggacgtcc tgcgcagta tattaagtcg 120  
 tcgatagaaa caagcattga aaggcacagc agtagtcaaa cagtgtgaaa cgctactggc 180  
 gccttacagc gcaaaaaggc tggcgactaa aaagtcacca gccatcagcc tgatttctca 240  
 ggctgcaacc ggaagggttg gcttatttaa ctccaacttc agcgccagct tcttcagag 300  
 cttttttcag tgcttctgcg tcgtctttgc tcacgccttc tttcagagca gccgggtgcag 360  
 attctaccag gtcttttagt tctttcagac ccaggccagt tgcg 404

<210> 411  
 <211> 152  
 <212> DNA  
 <213> Escherichia coli

<400> 411  
 agagcttttt tcagtgcctc tgcgtcgtct ttgctcacgc cttctttcaa gaggagcccg 60  
 gtgcagattc taccaggtct ttagcttctt tcagaccag gccagttgcg ccacgtactg 120  
 ctttgataac agcaacttg ttagcgccag ca 152

<210> 412  
 <211> 825  
 <212> DNA  
 <213> Escherichia coli

<220>  
 <221> misc\_feature  
 <222> (1)...(825)  
 <223> n = A,T,C or G

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 gaaaatggaa cactttccgc aatgcctgtt gctatcacgc ttaamccatt tcattgcat 120  
 ttacacagaa cggacgtcct gtcgcagtat attaagtcgt cgatagaaac aagcattgaa 180  
 aggcacagca gtagtcaaac agtgtgaaac gctactggcg ccttacagcg caaaaaggct 240  
 ggtgactaaa aagtcaccag ccacagcctt gatttctcag gctgcaaccg gaagggttg 300  
 cttatttaac ttcaacttca gcgcagcctt cttccagagc ttttttcagt gcttctgct 360  
 cgtctttgct cagccttctt ttcagagcag ccgggtgcag attctaccag gtcttttagt 420  
 tctttcagac ccaggccagt tgcgccagct actgctttga taacagcaac ttgttagcg 480  
 ccagcagctt tcagaattac gtcgaattca agttttttct tcagcagctt caaccgggccc 540  
 agcagctaca gctacagcag cagcagcggg aacaccgaat ttttcttyca ttggcagaga 600  
 tcaagttcta caacgtccat tacagacata gctgcaactg cttcaatgat tkgatcttwa 660  
 gtgatagaca tttaaattgt tcttgaatat cagaataagt ttatacgtaa gcgaatgcgt 720  
 taaaaagata actgcgatta agcagcttct ttgcgcatcg gtacagcagc cagaggtcga 780  
 accagtttgc cagccgaagg ttggcttttc agcctnnnn natta 825

<210> 413  
 <211> 425  
 <212> DNA  
 <213> Escherichia coli

<400> 413  
 agtagtcaaa caggtgkgra acgctactgg cgccttacag cgcaaaaagg ctggtgacta 60  
 aaaagtcacc agccatcarg ctgatttctc aggtctgaac ccggaagggt tggcttattt 120  
 aacttcaact tcagcgccag cttcttccag agcttttttc agtgcctctg cgtcgtcttt 180  
 gctcacgctt tctttcagag cagccgggtg agattctacc aggtcttttag cttcttccag 240  
 acccaggcca gttgcgccac gtagtctttt gataacagca actttgttag cgccagcagc 300  
 tttcagaatt acgtcgaatt cagttttttt ttcagcagct tcaaccgggc cagcagctac 360  
 agctacagca gcagcagcgg aaacaccgga atttttcttc cattgcagag atcaagttct 420  
 acaac 425

<210> 414  
 <211> 126  
 <212> DNA  
 <213> Escherichia coli

<400> 414  
 agagcttttt tcaagtgttc tgcgtcgtct ttgctcacgc cttctttcag agcagccggt 60  
 gcagattcta ccaggtcttt agcttctttc agaccacaggc cagttgcgcc acgtactgct 120  
 ttrata 126

<210> 415  
 <211> 264  
 <212> DNA  
 <213> Escherichia coli

<400> 415  
 ctgcmaccgg gargggttg cttattttaac ttcaacttca gcgccagctt cttycagagc 60  
 ttttttcaag tgcttctgcg tcgtcttttg tcacgccttc tttcagagca gccggtgcag 120  
 attctaccag gtcttttagct tctttcagac ccaggccagt tgcgccacgt actgctttga 180  
 taacagcaac tttgttagcg ccagcagctt tcagaattac gtcgaattca gttttttctt 240  
 cagcagcttc aaccgggcca gcag 264

<210> 416  
 <211> 201  
 <212> DNA  
 <213> Escherichia coli

<400> 416  
 cgcataccct gcagcatcgg cccgatggag atcaggtcgg cagaacgctg taccgctttg 60  
 taggtggtgt taccggtggt cagatccggg aagatgaaca cggtagcgcg acctgcaacc 120  
 ggagagttcg gcgctttgga tttcgcaacg tcagccatta ccgcagcgtc gtactgcagc 180  
 ggaccgtcga tcatcaggtc a 201

<210> 417  
 <211> 239  
 <212> DNA  
 <213> Escherichia coli

<400> 417  
 aattcagcag ttgacagtgg cataaacgta actggtgact tttgcccggc atgacgccgg 60  
 gcttttttta ttattccgtg acttccagcg tagtgaaggc aaacttctcg ccatcaaata 120  
 gccctgact ggtagtttt agcgcgggga tcaactggcag agaaagaaac gccatctgaa 180  
 taaacggctc atcgggtaac ggaccgcatt cacgggcggc ggctttcaag gcgtcaatt 239

<210> 418  
 <211> 223  
 <212> DNA  
 <213> Escherichia coli

<400> 418  
 ttcttttttt cgtcaacggt gtccagaatc attttattta cctcgggtac ttatgctgat 60  
 ttttattatt atggggaagg tgttatttat gagtttcatt tatgccgtaa cgacaatgaa 120  
 ctcggaatt agtataagca gcgcgagaat aataatcatt gtgcaaagtc taatttaatt 180  
 aatactattt aaatattatt ttgagcatat gcacataagg ttg 223

<210> 419  
 <211> 223  
 <212> DNA  
 <213> Escherichia coli

<400> 419

ttcttttttt	cgtcaacggt	gtccagaatc	attttattta	cctcgggtac	ttatgctgat	60
ttttattatt	atggggaagg	tggtatttat	gagtttcatt	tatgccgtaa	cgacaatgaa	120
ctcgggaatt	agtataagca	gcgcgagaat	aataatcatt	gtgcaaatgc	taatttaatt	180
aatactattt	aaatattatt	ttgagcatat	gcacataagg	ttg		223

&lt;210&gt; 420

&lt;211&gt; 212

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 420

aatagcgggt	atgcacgcct	ttcttttttt	cgtcaacggt	gtccagaatc	attttattta	60
cctcgggtac	ttatgctgat	ttttattatt	atggggaagg	tggtatttat	gagtttcatt	120
tatgccgtaa	cgmcaatgaa	ctcgggaatt	agtataagca	gcgcgagaat	aataatcatt	180
gtgcaaatgc	taatttaatt	aatactattt	aa			212

&lt;210&gt; 421

&lt;211&gt; 438

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 421

ccctgtaaat	tatcgcccgt	ggcataaaaa	ctgcgtccaa	acgccgtctt	tgccagcagc	60
caggccataa	atgccaccag	aattatcgtc	aaccaaccaa	ttgctgaaac	gccaagcagc	120
agcggggcgg	agagctgttt	cagttcggcg	ggtaaccctt	caatccattt	gccgccagtc	180
cacagcaaca	tgatgcctct	gtacaaccct	aacgtgccaa	gggtggcaac	aatggcaggg	240
atctttagcc	acgcgaccag	gacaccgttg	aaaaatcccc	cgagcaaacc	aagcagtaaa	300
gtcgcgacac	aagcaacagg	tagtgaatat	cctgcgttca	gtaacatccc	caacagcacc	360
gcgcacattc	cgggtaatcg	aaccccactt	gaaacatcaa	tattgsgsgt	aagcattwcc	420
aagcgttcgs	gcccattkg					438

&lt;210&gt; 422

&lt;211&gt; 682

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 422

aattcccggg	gatccgtcga	ccgtgcgctt	ccggttggtg	caaccgcgga	aatggcgcg	60
cggtaagtat	ggcgggggta	ttccttcccc	gttgaggaca	ccgggttgtc	aggttgacca	120
tacgcttaag	tgacaacccc	gctgcaacgc	cctctgttat	caattttctg	gtgacgtttg	180
gcggatcag	ttttactccg	tgactgctct	gccgcctttt	ttaaagtga	ttttgtgatg	240
tggtgaatgc	ggctgagcgc	acgcggaaca	gttaaaacca	aaaacagtgt	tatgggtgga	300
ttctctgtat	ccggcggtta	ttgttaactg	gttaacgtca	cctggaggca	ccaggcactg	360
catcacaaaa	ttcattgttg	aggacgcgat	aatgaaaacg	ttattaccaa	acgttaatac	420
gtctgaaggt	tgttttgaaa	ttggtgtcac	tatcagtaac	ccagtattta	ctgaagatgc	480
cattaacaag	agaaaacaag	aacgggagct	attaaataaa	atatgcattg	tttcaatgct	540
ggctcgttta	cgtctgatgc	caaaaaggatg	tgacacaatga	attcagcatt	tgtgcttggt	600
ctgacagttt	ttcttggttc	cggagagcca	gttgatattg	cagtcagtgt	tcacaggaca	660
atgcaggagt	gatgactgca	gc				682

&lt;210&gt; 423

&lt;211&gt; 600

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 423

ggggatccga	ttgtgactgc	tctgccgccc	tttttaaagt	gaattttgtg	atgtggtgaa	60
tgcggctgag	cgcacgcgga	acagttaaaa	ccaaaaacag	tggttatggg	ggattctctg	120
tatccggcgt	taattgttaa	ctgggttaacg	tcacctggag	gcaccaggca	ctgcatcaca	180
aaattcattg	ttgaggacgc	gataatgaaa	acgttattac	caaacgttaa	tacgtctgaa	240
ggttgctttg	aaattggtgt	cactatcagt	aaccaggtat	ttactgaaga	tgccattaac	300

aagagaaaac	aagaacggga	gctattaaat	aaaatatgca	ttgtttcaat	gctgggtcgt	360
ttacgtctga	tgccaaaagg	atgtgcacaa	tgaattcagc	atgtgtgctt	gttctgacag	420
tttttcttgt	ttccggagag	ccagttgata	ttgcagtcag	tggtcacagg	acaatgcagg	480
agtgtatgac	tgacagcaacc	gaacagaaaa	ttcccggtaa	ctgttacccg	gtcgataaag	540
ttattcacca	ggataaatatc	gaaatcccgg	caggtcttta	aacagttccg	taataaataa	600

&lt;210&gt; 424

&lt;211&gt; 100

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 424

gggatccagc	aagaagatgc	ggttgtaccg	tcatcacgca	gatgcgcaaa	gctactcagc	60
aactgacctt	tcttcgcaat	aagcacgcca	ttagcgtcat			100

&lt;210&gt; 425

&lt;211&gt; 465

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 425

tgcggtggtt	accttcaaca	tccgtaactt	tctggcggat	agtttcacgg	taagcaacct	60
gcgggtttacc	tacgttcgct	tcaacggtga	attcacgctt	catacgggtca	acgatgatgt	120
cgaggtgcag	ttcgcccata	cccgcgatga	tggtctggtt	agattcttcg	tcagtccata	180
cacggaaaga	cgggtcttct	ttagccagac	ggcccagagc	cagaccatt	tttccctggt	240
cagctttggt	tttcggttca	actgcgatgg	agattaccgg	ctcaggggaat	tccatacgtt	300
ccagaatgat	cggcgcaccc	gggtcacaca	gggtgtcacc	agtggttacg	tctttcagac	360
cgatagcagc	agcgatgtcg	cccgcgcgaa	cttctttgat	ctcttcacgt	ttgttagcgt	420
gcattctgaac	gatacgaccg	aaacgctcac	gtgcagcttt	cacgg		465

&lt;210&gt; 426

&lt;211&gt; 653

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(653)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 426

tgatcggtc	aagcagaact	ggtttcgctt	tcttaaagcc	ttctttaaag	gcgatagaag	60
cagccagttt	aaacgccagt	tcagaggagt	caacgtcatg	gtaagaaccg	aagtgcagac	120
gaatacccat	gtctactacc	gggtagcctg	ccagcggacc	tgctttcagc	tggttcctgga	180
tacctttatc	aacggccggg	atgtattcgc	cagggattac	accaccttta	atgtcgttga	240
tgaactcgta	gcctttcggg	tttgaacccg	gctccagcgg	gtacatgtcg	ataacaacat	300
gaccatactg	accacgacca	ccagactggt	tgcggtggtt	accttcaaca	tccgtaactt	360
tctggcggat	agtttcacgg	taagcaacct	gcgggtttacc	tacgttcgct	tcaacggtga	420
attcacgctt	catacgggtca	acgatgatgt	cgaggtgcag	ttcgccatac	ccgcgatgat	480
ggctgggtag	attcttcgct	agtcataaca	cggnaagacg	ggtcttnttt	agccagacgg	540
gccagagnca	gacccatttt	tttctggcag	ctttggnttc	ggtcaactgc	gatggaaata	600
cccgggtcaa	ggaattcata	cgtttcanaa	tgatcggggc	attccgggtc	aca	653

&lt;210&gt; 427

&lt;211&gt; 268

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 427

ctttcttaaa	gccttcttta	aaggcgatag	aagcagccag	tttaaaccgc	agttcagagg	60
agtcaacgtc	atggtaagaa	ccgaagtgcg	gacgaatacc	catgtctact	accgggtagc	120

ctgccagcgg	acctgcttcc	agctgttccct	ggataccttt	atcaacggcc	gggatgtatt	180
cgccagggat	tacaccacct	ttaatgtcgt	tgatgaactc	gtagcctttc	gggtttgaac	240
ccggctccag	cggttacatg	tcgataac				268

&lt;210&gt; 428

&lt;211&gt; 330

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 428

gttttgggga	gatgtaagg	ctaactctgaa	tggctgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgactcctc	tggtcttata	acacaaggaa	acgtacttaa	ggtgcgtccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaattg	catcaattaa	ataaatataa	tggcgtaag	gcttcccagt	300
aatataatta	atactctact	tccagagtag				330

&lt;210&gt; 429

&lt;211&gt; 465

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 429

gttttgggga	gatgtaagg	ctaactctgaa	tggctgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgactcctc	tggtcttata	acacaaggaa	acgtacttaa	ggtgcgtccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaattg	catcaattaa	ataaatataa	tggcgtaag	gcttcccagt	300
aatataatta	atactctact	tccagagtag	aatattaaat	tttatccgcg	tggtgcatca	360
gcacaaattt	atcccacac	tggtcttctg	tctcgacatg	cgccggatct	ttcacaaatag	420
tattggggat	cgggcacacc	ttctggcagg	ttggtgtctc	gtagt		465

&lt;210&gt; 430

&lt;211&gt; 379

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 430

aatctgaatg	gctgcattcc	ttgtttaagg	aaaaacgaat	gactgattgc	cgatacctga	60
ttaaacgggt	catcaaaaatc	atcattgctg	ttttacagct	gaccccttctg	ttctttataac	120
acaaggaaac	gtacttaagg	tgctgcgggt	gaaccagtcg	gacgcacctt	taataactat	180
aaataagtgt	ctgggcagat	actatataaa	ttacttagt	gaatgattat	gctaattgtca	240
tcaattaaat	aaatataatg	gcgttaaggc	ttcccagtaa	tataattaat	actctacttc	300
cagagttaga	tattaaattt	tatccgcgtg	gtgcatcagc	acaaatttat	cccacaactg	360
ttcttctgtc	tcgacatgc					379

&lt;210&gt; 431

&lt;211&gt; 443

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 431

aagatgatgt	gatgagaaa	tcaatttgaa	taagacaata	ttaagagcta	aaaaaatgtc	60
aaaaaacact	aaatcaaaaa	ataatggcat	tagaaaaat	aatgcaaaaa	cggaggtgaa	120
attagtttat	ttcaaatgag	gaaaatctcc	cggcgaaaaa	accgggagat	gaaagtgtga	180
tgggtatcaa	ataaacaaca	gaggagaaat	ttttaacgca	gccattcagg	caaatcgttt	240
aatcccattg	cctggcggat	aagttgcggc	ttaacgccag	gaagcgtgtc	ggccagtttc	300
aaaccaatat	cacgcagcag	ttttttcgcc	ggattggtac	cggaaaaacag	atcgcggaat	360
ccctgcatac	cagccagcat	caacgccgca	ctgtgcttgc	ggctacgctc	atagcgacgc	420
agataaatgt	actgcccgat	gtc				443

<210> 432  
 <211> 638  
 <212> DNA  
 <213> Escherichia coli

<400> 432  
 caggggggtt gttgtgggca atgatgcatt taagttatcg tctgcagata gaggagatat 60  
 tacaataaac aacgaatcag ggcatttgat agtcaatacc gcaattctat caggagatat 120  
 agtcactcta agaggaggag aaattagggt ggtattatag cttgtgcgcg ccatgattgg 180  
 cgcgcaattt aaacttagtg ctttacatcg ctattgtctt gatttctttg aattatttta 240  
 taaattaaaa aaacgactgt tatgtataag caaagggtccg aacgaaaaat acattccaaa 300  
 taaatgcttg cttaaacttc tatatccttc cccgaaaaat gacacataaa attgagatat 360  
 tccaaaaaga gatactacaa ataaagatgc ctttatttta ttatttctaa taaaaataga 420  
 agcaataaaa aataataaca atgatataaa tctaagtgtt ttaaatataat tgtcttttat 480  
 gtttagtaata gtcggttagta tgtttgattc tccatatatt acgtgtagtt ttttatatac 540  
 atggaaataa ttttctttat actgagacat cacaccatca tcaaattggaa gtttgaagat 600  
 ggtgcttggt ttgctaacca ataaaaagag tgcattcg 638

<210> 433  
 <211> 299  
 <212> DNA  
 <213> Escherichia coli

<400> 433  
 ctttacctgg catgatccac ttcgccagaa taccggcaat aagcccaaaa ataatccatg 60  
 acagaatgcc cattgtttcc tcacttatct gttttgcatt agcggggttag tcgctgataa 120  
 aaagcatagc acaacatcgg gagggcaaga tttgtgacga gcatcacgga ggtttttttg 180  
 cgatggcgca gaaattgcgc catcaacgat cagtgataat taccaaccac aaacatcatg 240  
 ttcgttttcc gtgtcataag aacgtacggt attcaccaga tcttttatca cttcagccg 299

<210> 434  
 <211> 388  
 <212> DNA  
 <213> Escherichia coli

<400> 434  
 gaaaaaggag gcaatatcgg gtaaaggcat tagcccgacg aatacgtcgg gctacaaata 60  
 ttattgtgct gcaggtgttt tagcgggttg ttgatccaca ggttctaact ggaagaccac 120  
 atcgacctga tcatcaaact gaatagcggc ctgctcgtaa gtttcttggg cggacaccgg 180  
 cgcggcatcg gctttcatca tccgcacccat tgggctgggc tgatagttgg aaacatggta 240  
 gcgcacgcta tataccggcc ccagtttacg atgaaagccg ttcgccagtt cctgcgcctg 300  
 atgaatcgcg ttatcaatcg ctgccttacg cgctttgtct ttataggcat ccggctgcgc 360  
 cacgcccagc gacacagaac gaattccc 388

<210> 435  
 <211> 351  
 <212> DNA  
 <213> Escherichia coli

<400> 435  
 ctatccttga tgaaaccgcg agcaaagata ggtgattacg tcatggtttt acagaaaatt 60  
 acagaaaaag gaggcaatat cgggtaaagg cattagcccg acgaatacgt cgggctacaa 120  
 atattattgt gctgcaggtg ttttagcggg ttgttgatcc acaggttcta actggaagac 180  
 cacatcgacc tgatcatcaa actgaatagc ggctgctcg taagtttcct gggcggacac 240  
 cggcgcggca tcggctttca tcatccgcac cattgggctg ggctgatagt tggaaacatg 300  
 gtagcgcacg ctatataaccg gccccagttt acgatgaaag ccgttcgccca g 351

<210> 436  
 <211> 762  
 <212> DNA  
 <213> Escherichia coli

<220>  
 <221> misc\_feature  
 <222> (1)...(762)  
 <223> n = A,T,C or G

<400> 436  
 aattatgaaa cactgtcttg aatcgtctga atgacgggca catttgcgag cacgcatcca 60  
 gtaataacac aggaaactat tttatctacg cgtttagcgat agactgcttg catggcgaaa 120  
 ggaggtaagc cgacgatttc agcgggacgc tgaacacggga aagccccctcc cgaggaagg 180  
 gccataaata aggaaagggg catgatgaag ctactcatca tcgtggtgct cttagtata 240  
 agcttccccg cttactaaga ctaccagggc gggggaaacc ccgctctacc ctactcctg 300  
 aaagtatgcc ttacacgataa gattgtcaat ccgcaggctt ttagtctgct gatcctgcc 360  
 gcaaatattc tttgcgagtc gttacgcaat aatcacagag gaaactattt tattcacgcg 420  
 ttagcgatag actgcattca gggcgaaagg aggtaagccg atgatttcag cgggacgctg 480  
 aaacgggaaa gcctctcccg gagaagaggg cttttaataa ggaaaggggt atgatgaagc 540  
 acgtcatcat actggtgata ctcttagtga ttagcttcca ggcttactaa gaacaccagg 600  
 gggaggggga aacctcttcc taaccctcac ttctgaaatt ggtgctatg acgtggcgt 660  
 tactgcttan cgctaccagt ttgtctgcc tggcggtgt aacgccagat cggtaaccgt 720  
 ttggatattt taatgaaagc cgacaaatca atcanctga cg 762

<210> 437  
 <211> 292  
 <212> DNA  
 <213> Escherichia coli

<400> 437  
 cacatttgcg agcacgcato cagtaataac acaggaaact attttatcta cgcgttagcg 60  
 atagactgct tgcattggcg aaggaggtaa gccgacgatt tcagcgggac gctgaaacgg 120  
 gaaagcccct cccgaggaag gggccataaa taaggaaagg gtcattgatga agctactcat 180  
 catcgtggtg ctttagtca taagcttccc cgcttactaa gactaccagg gcgggggaaa 240  
 ccccgctcta ccctcactcc tgaaagtatg cttcacgat aagattgtca at 292

<210> 438  
 <211> 631  
 <212> DNA  
 <213> Escherichia coli

<400> 438  
 atttacactt tttacgaaat catgggatca ctaacaaaat atcgcttgct agttatatgt 60  
 tatggcagga aagatatgag actgatatta cagatcccca aagtggagag tttatgacca 120  
 ttaaaaataa gatgttgctg ggtgcgcttt tgctggttac cagtgcgcc tgggccgcac 180  
 cagccaccgc gggttcgacc aatacctcgg gaatttctaa gtatgagtta agtagtttca 240  
 ttgctgactt taagcatttc aaaccagggg acaccgtacc agaaatgtac cgtaccgatg 300  
 agtacaacat taagcagtg cagttgcgta acctgcccgc gcctgatgcc gggacgcact 360  
 ggacctatat ggggtggcgcg tacgtgttga tcagcgacac cgacggtaaa atcattaaag 420  
 cctacgacgg tgagattttt tatcatcgct aaaaaaagcc ccctcatcat gagggggaaa 480  
 tgcagacacc ttgttatttt ttattattag ccacttgctc gtcttgcttg ttattagtcg 540  
 tatttcacgt tgattaatgc ggttgccctc agtgcgccag atttaacttt gtttgatcgc 600  
 tagacgtagt aactggctgt tatcggaatt g 631

<210> 439  
 <211> 566  
 <212> DNA  
 <213> Escherichia coli

<400> 439  
 tatggcagga aagatatgag actgatatta cagatcccca aagtggagag tttatgacca 60  
 ttaaaaataa gatgttgctg ggtgcgcttt tgctggttac cagtgcgcc tgggccgcac 120  
 cagccaccgc gggttcgacc aatacctcgg gaatttctaa gtatgagtta agtagtttca 180  
 ttgctgactt taagcatttc aaaccagggg acaccgtacc agaaatgtac cgtaccgatg 240

agtacaacat	taagcagtgg	cagttgcgta	acctgcccgc	gcctgatgcc	gggacgcact	300
ggacctatat	gggtggcgcg	tacgtgttga	tcagcgacac	cgacggtaaa	atcattaaag	360
cctacgacgg	tgagattttt	tatcatcgct	aaaaaaagcc	ccctcatcat	gagggggaaa	420
tgcagacacc	ttgttatttt	ttattattag	ccacttgctc	gtcttgcttg	ttattagtcg	480
tatttcacgt	tgattaatgc	ggttgcctcc	agtgcgccag	atttaacttt	gtttgtatcg	540
tagacgtagt	aactggctgt	atcgaa				566

&lt;210&gt; 440

&lt;211&gt; 339

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 440

cgtattcaca	tccttttgat	tggtgataac	atgcgaatcg	gtattatttt	tccggttgta	60
atcttcatta	cagcggtcgt	attttttagca	tggtttttta	ttggcggcta	tgctgccccg	120
ggagcataaa	gatgaaaaaa	acaacgatta	ttatgatggg	tgtggcgatt	attgtcgtac	180
tcggcactga	gctgggatgg	tggtaacgtc	acctctaaaa	aatagcaaag	gctgcctgtg	240
tgcagccttt	gtgcaattta	agcgtaaact	tttaatcttc	ctgtagataa	atagcacgac	300
aatcgacca	ataacggcaa	ccacgaagct	gccaaaatt			339

&lt;210&gt; 441

&lt;211&gt; 376

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 441

catgaatatt	taaaaaggaa	aacgacatga	aaccgaagca	cagaatcaac	attctccaat	60
cataaaaat	ttccgtggag	cattttatta	ttgaatatag	aggtttaact	ccggtaaaaa	120
acaaagaagc	attgaatgca	gggaaaaata	atatggccat	aaaaaacatc	gaaagaaact	180
cttttaattt	aacatgtaaa	cgcatggtta	atcctcatat	cacgggtgga	gtgttaagaa	240
catacataaa	tggagtcatg	ttttcccttt	tccattttatc	aagtccctgt	tgccgtttta	300
gtccatctct	aattgcatat	tttaattttt	ctgataaatg	gcattgagca	tcgatttcat	360
ttaaaacaac	tgtaca					376

&lt;210&gt; 442

&lt;211&gt; 446

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 442

ttacgatagc	tattagtaaa	aataataagag	ttagctgtat	tgttatgtct	gtggcgaaat	60
tgactacctt	cgtttttttg	attaagaatg	attttattat	cgtaagtaaa	attacatgaa	120
tatttaaaaa	ggaaaacgac	atgaaaccga	agcacagaat	caacattctc	caatcataaa	180
atattttccgt	ggagcatttt	attatttgaat	atagaggttt	aactccggtg	aaaaacaaag	240
aagcattgaa	tgcagggaaa	aataatatgg	ccataaaaaa	catcgaaaaga	aactctttta	300
atttaacatg	taaacgcacg	gttaatcttc	atatcacggg	tggagtgtta	agaacataca	360
taaatggagt	catgtttttc	cttttccatt	tatcaagttc	ctgttgccgt	tttagtccat	420
ctctaattgc	atattttta	at				446

&lt;210&gt; 443

&lt;211&gt; 388

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(388)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 443

tcaccccggt	gccgattttc	aggcatcctg	atttaactta	gcacccgcaa	cttaactaca	60
------------	------------	------------	------------	------------	------------	----



ggaaaaacaaa	gagataaatg	tctaatacctg	atgcaaatcg	agccgatttt	ttaatcttta	120
cggactttta	ccgccttgg	ttattaattg	caactgtnatc	cgggcgttcg	cccgttttaa	180
tcacaatagg	ctgtgtagcc	tgggcctgtt	tctctttcac	ccgcgccaga	gcggcagcaa	240
tcgcatcttt	atctttggct	gcaggttgaa	cggctgcgct	cttatgtcgt	tcaaggcgag	300
ccgctttttc	gcgctccaga	cgagcctggc	gcgcttcgaa	acgcgctttg	gcttctgcgg	360
cncgcttttc	ttcctgacga	atagccgc				388

&lt;210&gt; 444

&lt;211&gt; 209

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 444

aattttaata	acgctatctg	cggataaagc	agaatagggtg	gttaacccca	gacataaacc	60
gaggaaaata	atgttattgt	atttcataat	ctattgttcc	ttagcgacag	attgctgtct	120
gctggttcag	taaggtagca	ggagaaactt	caggaagctt	gtactcgaca	atacagtttg	180
agttttttatc	tttgcccat	gaaacctgt				209

&lt;210&gt; 445

&lt;211&gt; 341

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 445

catcctcaat	accgttaaat	gcaacccgaa	cccccgttgt	ccctttgctg	cattcactta	60
acgtaatctg	aaaagggacg	gctggacttg	tgctaccggt	cgttggaaat	tgtctggcac	120
tggtttttttg	gagatctacg	gtaaaattaa	gcgaatccga	tgagactgtg	cagccataat	180
cgaggacgcg	cccgctaatt	ttaataacgc	tatctgcgga	taaagcagaa	taggtgggta	240
accccgagaca	taaaccgagg	aaaataatgt	tattgtattt	cataatctat	tgttccttag	300
cgacagattg	ctgtctgctg	gttcagtaag	gtaccaggag	a		341

&lt;210&gt; 446

&lt;211&gt; 697

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 446

agattttactg	ccaattttccg	gcagatcgga	aagggttaam	ccatattgat	ccataagggt	60
acgaatcmcg	ggctataccg	ccaggcatgg	cttgagccat	ggcattaaat	tccgcaaatt	120
cgggcgctga	ttcttccac	gcggttattt	tggcacacac	cagatccagc	aagggtttt	180
caggatcggt	gagcagcaga	tgatctacca	gttcacgcgc	ctgggtgtat	tgttcctcgt	240
tctgaataacc	cgccagaaaa	ggtgccacag	cagttagctt	ttctcctgct	tgcaagatgt	300
cggcaatcgc	aatcattttt	tccccttagt	acgatgaaca	gcggtaaaga	aatcgatttc	360
tttatgcgtc	ataacttcac	gtatgtagca	cttttgcgat	tcaaaaaaga	ccattgctac	420
aacacgtaat	tcattgcccc	caacattgaa	aacataatgc	ttatccagat	atttgaagtt	480
atccagagat	gggaataactg	cttttaatga	ctcaggtttt	ttgaaatata	ccttagcaat	540
cgtgktcccc	agagccacca	actccgtttt	atgttgcggt	tatttttccg	cagcatcttt	600
caatgctttt	tgagttatca	ggtgcattct	tcatcacgtc	cgtkgmcaaa	ttggcaatat	660
gataacatcc	gttgccagat	tggcacggat	gaattat			697

&lt;210&gt; 447

&lt;211&gt; 215

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 447

aattaataac	ttttcgtttag	gcagtttttg	gtgtgagttg	caagagggga	gactactgaa	60
taactcaagt	tttataatcg	aggggaaaat	ggtgatggcg	ttcatagcaa	aacgccctca	120
accataaagg	tcgaggggcg	ttaagatgtt	aaaaacccgc	tatccgttaa	aaaacaatgt	180
tcaactaagg	tcagtgcacat	tgcgctaaaa	aagcg			215

<210> 448  
 <211> 395  
 <212> DNA  
 <213> Escherichia coli

<400> 448  
 gcattatttca tgagaaatgt gtatcgtaaa tcaactgaaa ttaacgcaac catttggtat 60  
 ttaaggttta attatctgtg tgtgatattt tattgaatgt tttaaatatt gtttttattg 120  
 gcattgctat aatattgggt atcatttgct gaatggattc agtcttaatg agtggggttt 180  
 taagggacag gcatagagta atgatacgtg tgcataacca acatctttac tcattatgtc 240  
 attgaatgtt gacgctatgt gtttatgagg gagaggtatt ttcagttgat ctggattgtt 300  
 aaattcatat aatgcgcctt tgctcatgaa tggatgccag tatgtagtgg gaaattataa 360  
 atattgaaat agtccaacta cttcttttatt accaa 395

<210> 449  
 <211> 641  
 <212> DNA  
 <213> Escherichia coli

<220>  
 <221> misc\_feature  
 <222> (1)...(641)  
 <223> n = A,T,C or G

<400> 449  
 ataatcaggt aagaaaaggt gcgcggagat taccgtgtgt tgcgatatat tttttagttt 60  
 cgcgtggcaa tacatcagtg gcaataaaac gacatatcca gaaaaatata cactaagtga 120  
 atgatattctt ccgatttatc ttaatcggtt atggataacg gcaaagggct tcgttttttc 180  
 ctatacttat tcagcactca caaataaagg aacgccaatg aaaattatac tctgggctgt 240  
 attgattatt ttcttgattg ggctactggg ggtgactggc gtattttaaga tgatatttta 300  
 aaattaatta atgtcatcag gtccgaaaat aacgagaata tttcagtcct tcctcctgtt 360  
 gcgctcctgt catgtgcatt gcttcatata atcactggcg caaggagcgc cgcaggcgna 420  
 gnntgcncgn cgnccacact naccccatgc cgaacttcag aantgaaaac nccntaacnc 480  
 cgatngtcgg cggnggcctc cccatgcnan agtangggaa ntgccangcg ncnntataaa 540  
 cgaaaggctn attncaaaga ctgggccttn cntttatctg atgtttgtcg gagaacgctc 600  
 tcctgagnan gacaaatncc gccggggagcg gatttgaacn t 641

<210> 450  
 <211> 314  
 <212> DNA  
 <213> Escherichia coli

<220>  
 <221> misc\_feature  
 <222> (1)...(314)  
 <223> n = A,T,C or G

<400> 450  
 gaactacgag taagaatagc tncgaattcc cgtttatgga taacggcaaa gggcttcggt 60  
 ttttcctata cttattcagc actcacaat aaaggaacgc caatgaaaat tatactctgg 120  
 gctgtattga ttattttcct gattgggcta ctgggtgtga ctggcgatt taagatgata 180  
 ttttaaaatt aattaatgtc atcaggtccg aaaataacga gaatatttca gtctctcatc 240  
 ctgtttgcgt cctgtcatgt gcattgcttc atataatcac tggcgcaagg agcgcgcagg 300  
 gggntntnnt cttt 314

<210> 451  
 <211> 236  
 <212> DNA  
 <213> Escherichia coli

<400> 451

atatacacta agtgaatgat atcttccgat ttatcttaat cgtttatgga taacggcaaa	60
gggcttcggt ttttccata cttattcagc actcacaat aaaggaacgc caatgaaaat	120
tatactctgg gctgtattga ttattttcct gattgggcta ctgggtgtga ctggcgtatt	180
taagatgata ttttaaaatt aattaatgtc atcaggtccg aaaataacga gaatat	236

&lt;210&gt; 452

&lt;211&gt; 418

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 452

cggagattac cgtgtgttgc gatatatattt ttagtttcgc gtggcaatac atcagtggca	60
ataaaacgac atatccagaa aaatatacac taagtgaatg atatcttcg atttatctta	120
atcgtttatg gataacggca aagggttcg ttttttcta tacttattca gcaactcaca	180
ataaaggaaac gccaatgaaa attatactct gggctgtatt gattattttc ctgattgggc	240
tactgggtgtg gactggcgta ttttaagatga ttttttaaaa ttaattaatg tcatcaggtc	300
cgaataaac gagaatattt cagtctctca tcctgttcg ctctgtcat gtgcattgct	360
tcatataatc actggcgcaa ggagcgcgca gggggcggcc aatcgccgcc gccccctg	418

&lt;210&gt; 453

&lt;211&gt; 551

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 453

aacaatttgc ccatgcgctc ggtcatgcgc tgcacgccc ggccattttg sgcgcccccg	60
cgaccgccat tcgactgtta atgggcgaat cttcagttact ggtattaggt ggacaacgcg	120
cgtgcctaa acggctggaa gaagcgggtt ttgcgtttcg ctggtacgat ttagaagagg	180
cgtggcgga tgtcgttcgc tgatgtggtt tacagcaaac atccgccagt taactcccgg	240
tgttacagga ttagtggtt tgcgcgataa gatcgtctgg tgaaagtcgg gtcaccatca	300
taactaactc tctgtctaaa cctctatcca gcatctcctg agcaatacgc agggcttctt	360
cgtgtttgcc ctgcattgcg ccttcttcac gtaatctgtc agcaatgggc atcaagtttc	420
tccttttctt gtgggtgcgcg ttccgctatc tcaccaataa atgcacgaaa acgctgggca	480
tcccctgttt gtaatacgtg attaaacagg gcttttagct gtctgtcatt agtgktccct	540
gtaactagca g	551

&lt;210&gt; 454

&lt;211&gt; 93

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 454

tggcatctcg gtgttgccga ttttcatgat atccagcccc cggaactt cttcccaaac	60
ggttttgcgt ttatccattg agtcacggaa ctg	93

&lt;210&gt; 455

&lt;211&gt; 232

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 455

cgtgccgaga tgatcctgta accatcatca gttgtgaagt agtgattcac gacttcaagg	60
cgtttttcaa aagggtattt tggctttgac atattagggg ctattccatt tcatcgcca	120
acaaaatggg tgcagtacat actcgttgga aatcaacaca ggaggctggg aatgccgcag	180
aaatatagat tactttcttt aatagtgatt tgtttcacgc ttttattttt ca	232

&lt;210&gt; 456

&lt;211&gt; 713

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

<220>  
 <221> misc\_feature  
 <222> (1)...(713)  
 <223> n = A,T,C or G

<400> 456

ttagnggatn	naangccac	ancctcgang	gatctaggag	gtagaatagc	ttcgaattcc	60
ccagcagagc	gcggccttct	tcgtcagatt	tcgcagtagt	ggtaattgga	atatccaaac	120
cacgaacgcg	gtcgacttta	tcgtagtcca	tttctgggaa	gatgatctgc	tcacggacac	180
ccatgctgta	gttaccacga	ccgtcgaaag	acttagcgga	caggccacgg	aagtcacgga	240
tacgaggtag	agcaatagtg	atcaggcgct	caaagaactc	ccacatgcgt	tcgccacgca	300
gagttacttt	acagccgata	ggatagccct	gacggatttt	gaagcctgca	acagatttgc	360
gtgctttggt	gatcagcggt	ttttgaccgg	agattgctgc	caggtctgct	gctgcttat	420
ccagcagttt	ttgtcagcg	atcgcttcac	caacacccat	gttcaggggt	atcttctcga	480
cccaggggac	ttgcatgaca	gaattgtagt	taaactcagt	catgagtttt	ttaactactt	540
cgtctttgta	gtaatcatgc	agtttcgcca	tcgtactact	ccatgctcgt	gaacgctctc	600
ctgagtagga	caaatccgcc	ggagccggat	ttaacgttgc	gaacaaccgn	cccggagggg	660
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<400> 457

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gtttttagtt	ttgcttaaaa	atattgttag	ttttattaaa	tgcaaaacta	aattattggt	180
atcatgaatt	tggtgtatga	tgaataaaat	ataggggggt	atagatagac	gtcattttca	240
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<210> 458  
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<400> 458

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taggtctgtt	aatggatttt	atttttacia	ttttttgtgt	ttaggcata	aaaaatcaac	240
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<210> 459  
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<400> 459

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aaagggttat	gatgaagctc	gtcatcatac	tgggtgtgtt	gttactgtta	agtttcccga	240
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<210> 460  
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<400> 460

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cccttacccct	tggttccttta	ctctaggttg	aaaaaacaac	agcgtcaata	ggcctgccat	240
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&lt;210&gt; 461

&lt;211&gt; 359

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 461

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&lt;210&gt; 462

&lt;211&gt; 673

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 462

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&lt;210&gt; 463

&lt;211&gt; 630

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 463

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&lt;210&gt; 464

&lt;211&gt; 391

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

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 aaaaaatttg agggataagg ccggaatggc tccggccaga gggaaagttaa ccgcgaagct 180  
 gttgctgctt gagggtcgtt ttaaccagac gccaggcgct ccatacggca aaaccgcgtc 240  
 tggcccagcg gaccagcata ttaggatggc gaatcgcca gatcgccatc acgctactgc 300  
 caaccagcgc ccaggagcgc agacttagca gcatattcca gcgacgatcg taagcgctg 360  
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 <211> 625  
 <212> DNA  
 <213> Escherichia coli

<400> 465  
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 gactaatgaa cggagataat ccttcaccta accggccctt tggtacagtt gtgtacaagg 180  
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 gccgggtccg ctcttccaat gaccacatcc agaggctctt caggaaatgc gcgactcaca 480  
 cctgctgtca cggtaatggt gatatgcctt tcagaatgtg tgatggcatg gttatcgact 540  
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 atgataaatt cttcgcccc gtagc 625

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 <211> 623  
 <212> DNA  
 <213> Escherichia coli

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 ctcaactgta agggatttga aatgttaaca caagctctcg ctgtaggggt atagccgaga 300  
 ccaccgaagc ccggagggtg tgaaataaaa ccgggcacaa cacgaaggcg catttccgat 360  
 atccataaag agtcggtctt gtctgttaaa tttaaatggt gggagtgcgc ctccgggtgt 420  
 aaataacgac attgctgtgt gtagtcctgg cggcatcagt tttttcttg aagttcgggt 480  
 gatgtccgcc ctttttaaa tgaattttgt gatgcggtga atgcggctaa gcgcacgtgg 540  
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 <212> DNA  
 <213> Escherichia coli

<400> 467  
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 agcatcttgt aaagccttta tcgtttttt atgctctgga ttaatataat cactacatct 180  
 atctgagcaa tctgttggtg atggacatgt caacccatgg tcatttacag ccaa 234

<210> 468  
 <211> 529  
 <212> DNA  
 <213> Escherichia coli

<400> 468  
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 atgaacaact gtccatgatt tcgtttaaga atgaagagaa atcactaaac gaactgaata 240  
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 ctccaactta ttgatagtgt tttatgttca gataatgcc gatgactttg tcatgcagct 360  
 ccaccgattt tgagaacgac agcgacttcc gtcccagccg tgccagggtgc tgcctcagat 420  
 tcagggttatg ccgctcaatt cgctgcgtat atcgcttttc cttatcagtt cgttgatgtc 480  
 agtggttttg accacgaggg agcttcacgc gagttattga aaaccctga 529

<210> 469  
 <211> 261  
 <212> DNA  
 <213> Escherichia coli

<400> 469  
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 gagttcaata taatgtttgt cttcaatttt tcttacttca gggtaatata gattgctcat 180  
 tacattgtga gcttcacatt tatttaattt tctgttgact ccagctctcc gtgataacgg 240  
 ttttataatt agatgcttat c 261

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 <211> 98  
 <212> DNA  
 <213> Escherichia coli

<400> 470  
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 ctttacgtac ttctgcgttg atagtaaaca tttctttc 98

<210> 471  
 <211> 259  
 <212> DNA  
 <213> Escherichia coli

<400> 471  
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 agctttagct tgcatgttca tgactttgtc gtgatccagc tcgatagcca gcggcgcttc 180  
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 cttaccctgc tctttacgt 259

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 <211> 94  
 <212> DNA  
 <213> Escherichia coli

<400> 472  
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<210> 473  
 <211> 174  
 <212> DNA  
 <213> Escherichia coli

<400> 473  
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174

<210> 474

<211> 138

<212> DNA

<213> Escherichia coli

<400> 474

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120

138

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<211> 191

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<213> Escherichia coli

<400> 475

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180

191

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<211> 245

<212> DNA

<213> Escherichia coli

<400> 476

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240

245

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<211> 319

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<213> Escherichia coli

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180

240

300

319

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<211> 149

<212> DNA

<213> Escherichia coli

<400> 478

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120

149

<210> 479

<211> 330

<212> DNA



&lt;213&gt; Escherichia coli

&lt;400&gt; 479

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accacgttc	gcggaaccag	cttgatctac	gtcaccacca	ccgaggtagt	tagcatcggt	300
ataggcgctg	aagttcttgg	tgaagctaaa				330

&lt;210&gt; 480

&lt;211&gt; 191

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 480

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aagctttttt	c					191

&lt;210&gt; 481

&lt;211&gt; 188

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 481

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gttcttca						188

&lt;210&gt; 482

&lt;211&gt; 172

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 482

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aaggattcga	ccactgccag	ttcttgcaaa	tcgtctttca	cgcgattaag	ca	172

&lt;210&gt; 483

&lt;211&gt; 266

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 483

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gttggttgaa	tggcgacggt	attgtcgaag	tcttttttgg	ttgcccccat	cttcagcgcc	240
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&lt;210&gt; 484

&lt;211&gt; 259

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 484

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&lt;210&gt; 485

&lt;211&gt; 73

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 485

caggtcggaa	cttacccgac	aaggaatttc	gctaccttag	gaccgttata	gttacggccg	60
ccgtttaaccg	ggg					73

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- (71) Applicant: ELITRA PHARMACEUTICALS, INC.  
[US/US]; Suite A, 3510 Dunhill Street, San Diego, CA 92121 (US).
- (72) Inventors: ZYSKIND, Judith; 8514 La Jolla Scenic Drive, La Jolla, CA 92047 (US). OHLSEN, Kari, L.; 3560 Vista De La Orilla, San Diego, CA 92117 (US). TRAWICK, John, D.; 7210 Baldrich Street, La Mesa, CA 91942 (US). FORSYTH, R., Allyn; 1135 Beryl Street, San Diego, CA 92109 (US). FROELICH, Jamie, M.; 5057 35th Street, San Diego, CA 92116 (US). CARR, Grant, J.; 2210 Sunrise Glen, Escondido, CA 92029 (US). YAMAMOTO, Robert, T.; 3725 Norte Dame Avenue, San Diego, CA 92131 (US). XU, H., Howard; 11142 Ivy Hill Drive, San Diego, CA 92131 (US).
- (74) Agent: REISMAN, Joseph, M.; Knobbe, Martens, Olson & Bear, LLP, 16th Floor, 620 Newport Center Drive, Newport Beach, CA 92660 (US).
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(54) Title: GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN *ESCHERICHIA COLI*

(57) Abstract: The sequences of nucleic acids encoding proteins required for *E. coli* proliferation are disclosed. The nucleic acids can be used to express proteins or portions thereof, to obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate molecules for rational drug discovery programs. The nucleic acids can also be used to screen for homologous genes that are required for proliferation in microorganisms other than *E. coli*. The nucleic acids can also be used to design expression vectors and secretion vectors. The nucleic acids of the present invention can also be used in various assay systems to screen for proliferation required genes in other organisms as well as to screen for antimicrobial agents.

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 00/02200

## A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, STRAND, BIOSIS, BIOTECHNOLOGY ABS, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	POST L E ET AL: "NUCLEOTIDE SEQUENCE OF THE RIBOSOMAL PROTEIN GENE CLUSTER ADJACENT TO THE GENE FOR RNA POLYMERASE SUBUNIT BETA IN ESCHERICHIA COLI" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA,US,NEW YORK, NY, vol. 76; no. 4, 1 April 1979 (1979-04-01), pages 1697-1701, XP000574791 abstract	1
A	WO 99 02673 A (DUGOURD DOMINIQUE ET AL.) 21 January 1999 (1999-01-21) page 7, line 25 -page 9, line 30 examples 2-6	1

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
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- \*O\* document referring to an oral disclosure, use, exhibition or other means
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\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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\*&\* document member of the same patent family

Date of the actual completion of the international search

31 October 2000

Date of mailing of the international search report

13. 11. 00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

De Kok, A

## INTERNATIONAL SEARCH REPORT

International Application No

PC 00/02200

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 21366 A (QBI ENTERPRISES LTD) 22 May 1998 (1998-05-22) page 8, line 9 - line 13 page 21, line 30 -page 25, line 2 page 26, line 11 -page 27, line 35 ---	
X	BLATTNER F R ET AL: "THE COMPLETE GENOME SEQUENCE OF ESCHERICHIA COLI K-12" SCIENCE., vol. 277, 5 September 1997 (1997-09-05), pages 1453-1462, XP002923023 LANCASTER, PA., US ISSN: 0036-8075 the whole document, especially figure 3 ---	8,9
X	VAN HEESWIJK W.C. ET AL.: "The genes of the glutamine synthetase adenylation cascade are not regulated by nitrogen in Escherichia coli" MOLECULAR MICROBIOLOGY, vol. 9, 1993, pages 443-457, XP000926027 OXFORD GB nt4271-4371 of glnE sequence 100% identical with ntl-100 of seq.id.165 abstract ---	9
A	LEE N.G. ET AL.: "Molecular cloning and characterization of the nontypable Haemophilus influenzae-2019 rfaE gene required for lipopolysaccharide biosynthesis" INFECTION AND IMMUNITY., vol. 63, no. 3, 1995, pages 818-824, XP000953326 WASHINGTON., US ISSN: 0019-9567 the whole document ---	8
A	AUSTIN A.E. ET AL.: "Genetic analysis of lipopolysaccharide core biosynthesis by Escherichia coli k12 insertion mutagenesis of the RFA locus" JOURNAL OF BACTERIOLOGY, vol. 172, 1990, pages 5312-5325, XP000926028 WASHINGTON US the whole document --- -/--	8

## INTERNATIONAL SEARCH REPORT

International Application No.

P US 00/02200

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>VALVANO M.A. ET AL.: "The rfaE gene from Escherichia coli encodes a bifunctional protein involved in biosynthesis of the lipopolysaccharide core precursor ADP-L-glycero-D-manno-heptose." JOURNAL OF BACTERIOLOGY, vol. 182, January 2000 (2000-01), pages 488-497, XP000926030 WASHINGTON US the whole document</p> <p>-----</p>	8

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/02200**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 11 13 34-45 47 48 50 51 53 55 57-63 65 67-93 95-105 107-110  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1-10, 12, 14-33, 46, 49, 52, 54, 56, 64, 66, 94 and 106, all partially
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11 13 34-45 47 48 50 51 53 55 57-63 65 67-93 95-105 107-110

In view of the large number and also the wording of the claims presently on file, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and concise), namely the nucleic acid sequences as identified in claims 1 and 8 respectively, sequences related to said sequences as well as their use. This corresponds to the subject-matter of claims 1-10, 12, 14-33, 46, 49, 52, 54, 56, 64, 66, 94 and 106.

It should be noted that since claim 46 has been searched, the subject-matter of claims 35-45 has been searched restricted to the gene products of claim 46, i.e. for those gene products for which (additional) search fees have been paid

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-7, 12, 49, 52, 56, 66, all partially

Invention 1:

A purified or isolated nucleic acid sequence consisting of SEQ.ID. No.: 405, a vector comprising said sequence, a host comprising said vector, the use of said sequence for inhibiting cellular proliferation, a composition comprising said sequence, the use of said sequence for inhibiting the expression of a gene and the use of said nucleic acid sequence for identifying bacterial strains.

2. Claims: 1-7, 12, 49, 52, 56, 66, all partially

Inventions 2 to 81:

Idem as invention 1, but for SEQ.ID.NO's 406-485 respectively

3. Claims: Claims 8-10,12,14-33,46,54,64,66,94 and 106,  
all partially:

Invention 82:

A purified or isolated nucleic acid consisting of SEQ.ID.No.: 82, a vector comprising said nucleic acid sequence, a host comprising said vector, a polypeptide encoded by said nucleic acid sequence and having the sequence of SEQ.ID.No.: 243, an antibody binding said polypeptide, a method for producing said polypeptide, a method for identifying compounds influencing the activity of said polypeptide, a method for identifying compounds influencing the level of said polypeptide, a method for inhibiting the expresion of said nucleic acid, the use of said nucleic acid sequence for identifying bacterial strains and the use of said nucleic acid sequence for identifying proliferation inhibitors.

4. Claims: Claims 8-10,12,14-33,46,54,64,66,94 and 106,  
all partially:

Inventions 83 to 242:

Idem as invention 82, but for SEQ.ID.No's 83-88, 90-242 (and their corresponding polypeptide sequences, see Table II) respectively.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP98/00/02200

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9902673	A	21-01-1999	AU	8327798 A	08-02-1999
			EP	1025219 A	09-08-2000
<hr/>					
WO 9821366	A	22-05-1998	AU	5442198 A	03-06-1998
			EP	0960212 A	01-12-1999
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